Complete Summary

GUIDELINE TITLE

Chemotherapy and biotherapy: guidelines and recommendations for practice.

BIBLIOGRAPHIC SOURCE(S)

Oncology Nursing Society (ONS). Chemotherapy and biotherapy: guidelines and recommendations for practice. Pittsburgh (PA): Oncology Nursing Society (ONS); 2001. 226 p.

GUIDELINE STATUS

Note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- On August 31, 2005, Genentech and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of updated cardiotoxicity information related to the use of Herceptin (trastuzumab), obtained from the National Surgical Adjuvant Breast and Bowel Project (NSABP) study (B-31), a randomized, Phase III trial that was conducted in 2043 women with operable, HER2 overexpressing breast cancer (IHC 3+ or FISH+). This study demonstrated a significant increase in cardiotoxicity in patients who were randomized to the Herceptin-containing arm as compared to patients who received chemotherapy alone. See the FDA Web site for more information.
- On January 26, 2006, Bristol-Myers Squibb notified healthcare professionals about revisions to the WARNINGS and ADVERSE REACTIONS sections of the prescribing information to describe cutaneous vasculitic toxicities, including vasculitic ulcerations and gangrene, in patients with myeloproliferative disorders during therapy with hydroxyurea, most often reported in patients with a history of or currently receiving interferon therapy. The PRECAUTIONS and DOSING AND ADMINISTRATION sections have been revised to provide updated information on the safe handling of these products. The proposed changes are highlighted in â œDear Healthcare Providerâ letters issued January 2006 by Bristol-Myers Squibb; specific wording of these additions and revisions to the labeling is pending U.S. Food and Drug Administration (FDA) review and approval. See the FDA Web site for more information.

- On March 15, 2006, Ligand Pharmaceuticals and the U.S. Food and Drug Administration (FDA) notified healthcare professionals of changes to the WARNINGS section of the prescribing information for Ontak (denileukin diftitox), indicated for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma. Loss of visual acuity, usually with loss of color vision, has been reported following administration of Ontak. While recovery was reported in some of the affected patients, most patients reported persistent visual impairment. See the FDA Web site for more information.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Cancer

GUIDELINE CATEGORY

Evaluation
Management
Treatment

CLINICAL SPECIALTY

Nursing
Oncology

INTENDED USERS

Advanced Practice Nurses
Nurses

GUIDELINE OBJECTIVE(S)

Overall Objective

- To provide the registered nurse with the clinical information necessary to administer cytotoxic and biotherapeutic agents

Specific Objectives

- To describe historical advances related to the use of cytotoxic therapeutic agents as treatment modalities
- To describe the investigational process all drugs undergo to gain U.S. Food and Drug Administration (FDA) approval
- To define the role of the nurse who cares for a patient receiving standard therapy, high-dose or dose-intense regimens, and investigational cytotoxic drugs
- To identify the importance of the cell cycle and cellular kinetics as they relate to the various classifications of cytotoxic agents
- To explain the goals of cancer therapy
- To cite the methods of measuring tumor response to therapy and identifying possible reasons for treatment failure
- To describe the safety precautions necessary when handling cytotoxic agents
- To identify the procedures for administering cytotoxic and therapeutic agents as part of cancer treatment
- To identify nursing interventions appropriate for a patient receiving cytotoxic therapies
- To identify acute, subacute, and chronic toxicities that can occur with the use of cytotoxic and therapeutic agents for cancer treatment
- To identify information pertinent to the comprehensive documentation of cytotoxic therapies

TARGET POPULATION

Biotherapy

- Adults (unless otherwise specified) with cancer receiving biotherapy

Chemotherapy

- Adults or children with cancer receiving chemotherapy
- Nurses administering chemotherapeutic agents

INTERVENTIONS AND PRACTICES CONSIDERED

1. Therapeutic use of chemotherapeutic and biotherapeutic agents, including proper storage, labeling, handling, and administration.

   Chemotherapeutic agents include:

   - Antimetabolites (Cytarabine [cytosine arabinoside, araC, Cytosar-U], Fluorouracil [5-FU], Floxuridine [FUDR], Mercaptopurine [6-MP, Purinethol], Methotrexate [MTX, Mexate], Thioguanine [6-thioguanine, 6-TG], Fludarabine [Fludara], Capecitabine [Xeloda], Deoxycoformycin [pentostatin, Nipent], Gemcitabine [Gemzar])

- Vinca alkaloid (Vinorelbine [Navelbine], Vincristine [Oncovin], Vinblastine [Velban])
- Epipodophyllotoxins (Etoposide [VP-16, Etopophos, VePesid], Teniposide [VM-26, Vumon])
- Taxanes (Paclitaxel [Taxol], Docetaxel [Taxotere])
- Camptothecins (Topotecan [Hycamtin], Irinotecan [Camptosar])
- Miscellaneous agents (Asparaginase [Elspar], Pegaspargase [Oncaspar], Hydroxyurea [Hydrea, Mylocel], Procarbazine [Matulane], Imatinib mesylate [Gleevec])
- Alkylating agents (Busulfan [Myleran], Melphalan [Alkeran], Carboplatin [Paraplatin], Cisplatin [Platinol], Cyclophosphamide [Cytoxan], Dacarbazine [DTIC], Ifosfamide [Ifex], Mechlorethamine hydrochloride [nitrogen mustard, Mustargen], Thiotepa [Thioplex], Chlorambucil [Leukeran])
- Antitumor antibiotics (Bleomycin [Blenoxane], Dactinomycin [actinomycin D, Cosmegen], Daunorubicin [daunomycin, Cerubidine], Doxorubicin [Adriamycin], Idarubicin [Idamycin], Mitomycin-C [Mutamycin], Mitoxantrone [Novantrone], Plicamycin [Mithracin])
- Hormonal therapy (Glucocorticoids: prednisone, hydrocortisone, Solu-Medrol, dexamethasone [Decadron]; Estrogens: chlorotrianisene [TACE], diethylstilbestrol [DES], estramustine [Emcyt], Estratab, estradiol; Aromatase inhibitor: anastrozole [Arimidex]; Antiestrogen: tamoxifen [Nolvadex]; Progestins: medroxyprogesterone acetate [Depo-Provera], megestrol acetate [Megace], LHRH analogs [Leuprolide [Lupron], goserelin acetate [Zoladex]; Bicalutamide [Casodex]; Flutamide [Eulexin])
- Nitrosoureas (Carmustine [BCNU]; Lomustine [CCNU]; Streptozocin [Zanosar])

Biologic agents include:

- Adoptive immunotherapy (Lymphokine-activated killer [LAK] cells, Tumor-infiltrating lymphocytes [TILs])
- Hematopoietic growth factors (Erythropoietin: Epoetin alfa [Epogen, Procrit]; Granulocyte-colony stimulating factor [G-CSF]; filgrastim [Neupogen]; Human granulocyte-colony stimulating factor; Granulocyte macrophage-colony stimulating factor [GM-CSF]: sargramostim [recombinant GM-CSF], products derived from yeast: Leukine; macrophage-colony stimulating factor [M-CSF]; Interleukin 11 [IL 11], oprelvekin [Neumega])
- Interferons (Interferon Alfa: interferon alfa-2a [Roferon-A], interferon alfa-2b [Intron-A], pegylated interferon [Pegasys], Interferon alfa-n3 [Alferon N], interferon alfacon-1 [Infergen]; Interferon beta: interferon beta-1a [Avonex], interferon beta-1b [Betaseron]; interferon gamma: interferon gamma-1b [Actimmune])
- Interleukins (Interleukin-1 [IL-1]: interleukin 1-alpha, interleukin 1-beta; interleukin-2 [IL-2]: aldesleukin [Proleukin]; interleukin-3 [IL-3]; interleukin-4 [IL-4]; interleukin-6 [IL-6]; interleukin-12 [IL-12]
- Levamisole (Ergamisol)
- Monoclonal antibodies (OncoScint, capromab pendetide [ProstaScint], trastuzumab [Herceptin], rituximab [Rituxan], gemtuzumab ozogamicin [Mylotarg])

- Fusion protein: denileukin diftitox (Ontak)
- Tumor necrosis factor
- Vaccines
- Gene therapy

2. Appropriate selection and use of antiemetic agents to control chemotherapy-induced nausea and vomiting
    - Serotonin antagonist (ondansetron, granisetron, dolasetron)
    - Dopamine antagonist (metoclopramide, prochlorperazine, droperidol, haloperidol, dronabinol, dexamethasone, lorazepam)
    - Cannabinoid (dronabinol)
    - Corticosteroid (dexamethasone)
    - Anxiolytic (lorazepam)
3. Patient preparation (education and informed consent) and pre-treatment assessment
4. Assessment of patient during treatment and post-treatment for adverse effects, complications, and response to treatment
5. Nursing management of general side effects of therapy, adverse reactions, or toxicities
6. Patient and family education

MAJOR OUTCOMES CONSIDERED

Safe administration of cytotoxic and biotherapeutic agents

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches using Medline, CINAHL (Cumulative Index to Nursing and Allied Health), and Index Medicus.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline document was reviewed by field reviewers.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary. The recommendations that follow are based on the previous version of the guideline.

Pharmacology of cytotoxic agents

A. Chemotherapeutic drugs: These drugs are classified according to pharmacologic action or effect on cell reproduction. See Table 4 in the original guideline document and modified and presented below.
    1. Cell-cycle specific drugs exert effect within a specific phase of the cell cycle.
        a. These drugs have the greatest tumor-cell kill when given in divided doses or as a continuous infusion with a short cycle time.
        b. Classifications include antimetabolites, plant alkaloids, and miscellaneous agents.
    2. Cell-cycle nonspecific drugs exert effect in all phases of the cell cycle, including the G_0 resting phase.

a. Cell-cycle nonspecific drugs also are effective in treating tumors with relatively few dividing cells.
b. If the cancer is sensitive to the agent used, cell kill is directly proportional to the amount of drug administered.
c. Classifications include alkylating agents, antitumor antibiotics, hormonal therapy, and nitrosourea agents.

B. Biotherapeutic drugs: See Table 5 in the original guideline document and modified and presented below.

Table 4. Characteristics of Cytotoxic Agents

A. Antimetabolites

Medication Names

1. Cytarabine cytosine arabinoside, araC, Cytosar-U)
   Nursing Considerations
   - Determine if the ordered dose is a standard dose or a high dose; administer the agent according to institution guidelines.
   - Cytarabine may be administered intrathecally.
   - For intrathecal (IT) administration: Use preservative-free saline.
2. Fluorouracil (5-fluorouracil, 5-FU)
   Nursing Considerations
   - Ensure that patient takes year-round photosensitivity precautions; encourage sunscreen use if patient must be exposed.
   - Leucovorin often is given concurrently.
3. Floxuridine (FUDR) Not used in pediatrics.
   Nursing Considerations
   - Recommendations about dose reduction apply to patients with compromised liver function. Adjust dose per institution protocol and monitor patient´s hepatic function carefully.
4. Mercaptopurine (6-MP, Purinethol)
   Nursing Considerations
   - Reduce oral dose by 75% when used concurrently with allopurinol. Patient should take drug on an empty stomach, 1 hr. before meals or 2 hr. after meals.
5. Methotrexate (MTX, Mexate)
   Nursing Considerations
   - High doses must be followed by leucovorin and vigorous hydration. Follow dosing schedule carefully.
   - Monitor serum methotrexate levels until 0.1 mmol.
   - Mouth care is necessary.
   - Take photosensitivity precautions.
   - Ensure that the patient avoids multivitamins with folic acid.
6. Thioguanine (6-thioguanine, 6-TG)
   Nursing Considerations
   - No dose reduction is necessary when this drug is used concurrently with allopurinol.
7. Fludarabine (Fludara)
   Nursing Considerations

- Administer this drug as a 30-min. infusion.
- Fludarabine has been used experimentally as a continuous infusion.
- Monitor pulmonary function tests.

8. Capecitabine (Xeloda) Not used in pediatrics.
   Nursing Considerations
   - Patient education regarding toxicity reporting and dose reduction is critical.
9. Deoxycoformycin (pentostatin, Nipent) Not used in pediatrics.
   Nursing Considerations
   - Administer this drug with 500 cc-1 $ID_5$1/2NS solution prior to the infusion and 500 cc $D_5$1/2NS solution postinfusion.
10. Gemcitabine (Gemzar) Not used in pediatrics.
    Nursing Considerations
    - Use with normal saline only.
    - Infuse over 30 min.; infusion longer than 60 min. or more than weekly can increase toxicity.
    - Myelosuppression is a dose-limiting toxicity.

B. Vinca alkaloids

Medication Names

1. Vinorelbine (Navelbine) Not used in pediatrics.
   Nursing Considerations
   - Vinorelbine is a vesicant.
   - Administer via IV push over 6-10 min. through the side port of a free-flowing IV, then flush with 75-125 cc solution.
2. Vincristine (Oncovin)
   Nursing Considerations
   - Vincristine is a vesicant; with extravasation, local tissue necrosis occurs.
   - Neurotoxicity is cumulative but often reversible; conduct a neuro evaluation before each dose. Withhold dose if severe paresthesia, motor weakness, or other abnormality develops.
   - Reduce dose in the presence of significant liver disease.
   - Stool softeners and/or a stimulant laxative may help prevent severe constipation.
   - Pediatrics: Acetaminophen or a narcotic is used for jaw pain.
3. Vinblastine (Velban)
   Nursing Considerations
   - Vinblastine is a vesicant.
   - Generally, neurotoxicity occurs less frequently with vinblastine than with vincristine; however, it can occur with high doses of vinblastine.

C. Epipodophyllotoxins

Medication Names

1. Etoposide (VP-16, Etopophos, VePesid)
   Nursing Considerations
   - Do not administer this drug by means of rapid IV infusion. Infuse it over 30-60 min. to avoid hypotension; monitor

patient´s blood pressure during infusion.
- Prior to use, dilute the drug to a final concentration of 0.2-0.4 mg/ml to prevent precipitation. Monitor for crystallization during infusion.
- Etoposide is soluble.
- Etopophos is a phosphorylated drug that can be given as a rapid IV push. Such a use is controversial if the patient is less than 1 year old.
- Etoposide is associated with the development of secondary malignancies.
- If a patient has had an allergic reaction to etoposide, premedicate him or her with diphenhydramine.

2. Teniposide (VM-26, Vumon)
   Nursing Considerations
   - Do not administer this drug via rapid infusion. Infuse it over 30-60 min. to avoid hypotension; monitor patient´s blood pressure during infusion.
   - Drug may cause an allergic reaction.
   - Administer through non-polyvinyl chloride (PVC) tubing.

D. Taxanes

Medication Names

1. Paclitaxel (Taxol) Not used in pediatrics.
   Nursing Considerations
   - Pretreat as follows to help prevent hypersensitivity reactions, including anaphylaxis: cimetidine 300 mg IV 30-60 min. before treatment, and diphenhydramine 50 mg IV 30-60 min. before treatment, and (unless contraindicated) dexamethasone 20 mg IV 30-60 min. before treatment.
   - Filter paclitaxel with 0.2-micron in-line filter.
   - Use glass bottles or non-PVC (polyolefin or polypropylene) bags to administer paclitaxel; do not use paclitaxel with PVC bags or PVC tubing.
   - Paclitaxel is an irritant. Extravasation may lead to local pain, edema, and erythema at the infusion site but not to skin necrosis.
2. Docetaxel (Taxotere) Not used in pediatrics.
   Nursing Considerations
   - Premedicate as follows to reduce the severity of hypersensitivity reactions and fluid retention: dexamethasone 8 mg PO BID, beginning one day prior to docetaxel treatment and continuing for the day of treatment and one day after.
   - Refer to institution guidelines for additional pretreatment requirements.
   - Do not use PVC tubing or bags to administer docetaxel.

E. Camptothecins

Medication Names

1. Topotecan (Hycamtin)
   Nursing Considerations

- Prior to administration, dilute the appropriate volume of reconstituted solution with either 0.9% sodium chloride IV solution or 5% dextrose IV solution.

2. Irinotecan (Camptosar)
   Nursing Considerations
   - This drug can cause early and late diarrhea, which can be dose limiting. Early diarrhea can occur within 24 hr. of administration and is generally cholinergic. Many institutions use atropine to treat this early diarrhea. Refer to institution protocol regarding the dosing and administration of atropine and other antidiarrheals.

F. Miscellaneous agents

Medication Names

1. Asparaginase (Elspar)
   Nursing Considerations
   - To prevent hypersensitivity reactions, including anaphylaxis, administer an intradermal test dose before the initial dose of asparaginase. Repeat the test if a week or longer passes between doses.
   - Giving the drug IM greatly reduces the incidence of anaphylaxis.
   - Pediatrics: Keep medications to treat anaphylaxis at bedside.
2. Pegaspargase (Oncaspar)
   Nursing Considerations
   - No need for test dose.
   - Presents less risk of anaphylaxis than does asparaginase.
3. Hydroxyurea (Hydrea, Mylocel)
   Nursing Considerations
   - Adjust the dose according to blood counts; do not change the dose too frequently. Frequent change results in response delay.
4. Procarbazine (Matulane)
   Nursing Considerations
   - Patient should avoid foods high in tyramine, because to some degree procarbazine inhibits monoamine oxidase.
5. Imatinib mesylate (Gleevec)
   Nursing Considerations
   - Weigh the patient frequently and monitor him or her for signs and symptoms of fluid retention (e.g., rapid weight gain, peripheral edema).
   - Ensure that the patient takes imatinib mesylate with food.
   - Monitor patient´s CBC differential and liver function tests.
   - Drugs that may increase plasma concentration include ketoconazole, itraconazole, erythromycin, clarithromycin.
   - Drugs that may decrease plasma concentration include dexamethasone, phenytoin, carbamazepine, rifampicin, phenobarbital, and St. John´s wort.
   - Interaction is possible if patients are receiving warfarin.
   - Advise women of childbearing age not to become pregnant while taking imatinib mesylate. Researchers have not conducted studies of the drug in pregnant women.

- Pediatrics: No data are available about the pediatric use of imatinib mesylate.

G. Alkylating agents

Medication Names

1. Busulfan (Myleran)
   Nursing Considerations
   - Monitor the patient´s blood count closely. If the leukocyte count is < 15,000/mcl, discontinue the drug.
   - Administer seizure prophylaxis.
2. Melphalan (Alkeran) Not commonly used in pediatrics.
   Nursing Considerations
   - Melphalan IV is a vesicant.
   - Myelosuppression may be delayed and last 4-6 weeks, so monitor blood counts carefully. Hold or reduce dose per institution protocol.
3. Carboplatin (Paraplatin)
   Nursing Considerations
   - Carboplatin exhibits much less renal toxicity than does cisplatin, so rigorous hydration is unnecessary.
   - Monitor the patient´s blood counts closely and reduce the dose per protocol.
4. Cisplatin (Platinol)
   Nursing Considerations
   - Cisplatin has vesicant potential if > 20 cc 0.5 mg/ml is extravasated. If less, cisplatin is an irritant.
   - Hold the drug if the patient´s serum creatinine is > 1.5 mg/dl; otherwise, irreversible renal tubular damage may occur. Amifostine may be used as a renal protectant.
   - Rigorous hydration is necessary to prevent nephrotoxicity. Use mannitol to achieve osmotic diuresis.
   - Obtain a baseline audiogram.
5. Cyclophosphamide (Cytoxan)
   Nursing Considerations
   - Give the dose, whether IV or oral, early in the day.
   - Adequately hydrate the patient. If the dose is oral, have the patient drink plenty of fluids.
   - Have the patient empty his or her bladder frequently to prevent hemorrhagic cystitis.
   - Pelvic irradiation potentiates hemorrhagic cystitis.
   - When used with irradiation, potential for radiation recall exists with subsequent doses of cyclophosphamide.
6. Dacarbazine (DTIC)
   Nursing Considerations
   - Dacarbazine is an irritant.
   - Administer by infusion over 30-60 min.
   - Dacarbazine can cause severe pain and burning at the injection site and along the course of the vein. To reduce these effects, increase the diluent, reduce the infusion rate, and apply cold compresses to the needle-insertion site and along the vein.
   - Protect solution from light (pink solution indicates

decomposition).
- Flu-like syndrome may occur up to 7 days after drug administration. Treat symptoms.
- Reduce doses for patients with poor renal function.

7. Ifosfamide (Ifex)
   Nursing Considerations
   - Administer the drug over 30 min. or more.
   - To prevent hemorrhagic cystitis, always administer ifosfamide with mesna. Mesna may be given as a bolus dose, continuous infusion, or mixed in the bag with the ifosfamide. Mesna dose should be 60%-100% of the ifosfamide dose (based on weight).
8. Mechlorethamine hydrochloride (nitrogen mustard, Mustargen)
   Nursing Considerations
   - Drug is a vesicant.
   - Administer the agent over several minutes, through the side arm of a free-flowing IV.
   - Flush with 125-150 cc normal saline.
   - If extravasation occurs, the antidote is sodium thiosulfate.
   - Use mechlorethamine as soon after preparation as possible (15-30 min.); it is extremely unstable.
   - Do not mix mechlorethamine with any other drug.
9. Thiotepa
   Nursing Considerations
   - Thiotepa is primarily excreted in the urine; monitor renal function carefully.
   - Take skin-care measures when using high-dose therapy.
10. Chlorambucil (Leukeran) Not used in pediatrics.
    Nursing Considerations
    - Toxicity may increase if the patient has used barbiturates.

H. Antitumor antibiotics

Medication Names

1. Bleomycin (Blenoxane)
   Nursing Considerations
   - Lymphoma patients have a higher incidence of anaphylaxis after receiving bleomycin than do other patients who receive bleomycin. Therefore, administer a test dose of 1-2 u IV, IM, or SQ before administering the first dose of bleomycin to a lymphoma patient.
   - Ensure that the patient and family understand the lifelong necessity of disclosing previous use of bleomycin when future needs for anesthesia occur.
   - Because of the dose-related incidence of pulmonary fibrosis, the cumulative lifetime dose should not exceed 400 u.
2. Dactinomycin (actinomycin D, Cosmegen)
   Nursing Considerations
   - Dactinomycin is a vesicant.
   - This drug may be ordered in mcg, so check the dose carefully.
3. Daunorubicin (daunomycin, Cerubidine)
   Nursing Considerations
   - Daunorubicin is a vesicant.

- Test the patient´s cardiac ejection fraction via multiple-gated acquisition (MUGA) scan before starting daunorubicin therapy.

4. Doxorubicin (Adriamycin)
   Nursing Considerations
   - Doxorubicin is a vesicant.
   - Doxorubicin may cause a flare reaction.
   - Test the patient´s cardiac ejection fraction via MUGA scan before starting doxorubicin therapy.
   - Do not exceed a lifetime cumulative dose of 550 mg/m^2 (450 mg/m^2 if the patient has had prior chest irradiation or concomitant cyclophosphamide treatment).
   - Initiate dexrazoxane for patients who have received a cumulative dose of 300 mg/m^2 and are continuing doxorubicin treatment. In pediatrics, dexrazoxane and doxorubicin may be used concurrently.
5. Idarubicin (Idamycin)
   Nursing Considerations
   - Idarubicin is a vesicant.
   - The cardiac toxicity of idarubicin is less than that of daunorubicin. Cumulative doses > 150 mg idarubicin are associated with decreased ejection fraction.
   - Local reactions (e.g., hives at injection site) may occur.
6. Mitomycin-C (Mitomycin)
   Nursing Considerations
   - Mitomycin-C is an irritant.
   - Nadir occurs 4-8 weeks after treatment begins.
   - Acute shortness of breath and bronchospasm can occur very suddenly when this drug is given with a vinca alkaloid.
7. Mitoxantrone (Novantrone)
   Nursing Considerations
   - Some sources classify mitoxantrone as a vesicant; others, as an irritant.
   - The cardiac toxicity of mitoxantrone is less than that of doxorubicin, but prior anthracycline use, chest irradiation, or cardiac disease can increase the patient´s risk.
8. Plicamycin (Mithracin) Not used in pediatrics.
   Nursing Considerations
   - The most significant toxicity associated with plicamycin is a bleeding syndrome that usually begins with an episode of epistaxis.
   - Monitor the patient´s blood counts, especially platelet counts.
   - Administer the drug over 30 min. to reduce gastrointestinal (GI) toxicity.

I. Hormonal therapy

Medication Names

1. Glucocorticoids: prednisone, hydrocortisone, Solu-Medrol, dexamethasone (Decadron)
   Nursing Considerations
   - Stress the importance of maintaining the steroid schedule.
   - Glucocorticoid therapy masks infection and hypokalemia.

- Educate the patient and family about the importance of following a low-sodium diet.
- After prolonged use of prednisone or dexamethasone, taper the dose to discontinue use; otherwise, prednisone can cause cardiac overload.

2. Estrogens: chlorotrianisene (TACE), diethylstilbestrol (DES), estramustine (Emcyt), Estratab, estradiol Not used in pediatrics.
   Nursing Considerations
   - Monitor women who have an intact uterus for signs of endometrial cancer.
   - Ensure that, during treatment, the patient does not eat foods containing calcium.
   - Use with caution for patients with cerebrovascular disease, diabetes, or hypertension.
3. Aromatase inhibitor: anastrozole (Arimidex)
   Nursing Considerations
   - Pediatrics: Safety and efficacy have not been established regarding pediatric use.
4. Antiestrogen: tamoxifen (Nolvadex) Not used in pediatrics.
   Nursing Considerations
   - Adverse reactions are relatively mild and rarely severe enough to require discontinuation of treatment.
5. Progestins: medoxyprogesterone acetate (Depo-Provera), megestrol acetate (Megace)
   Nursing Considerations
   - At least 2 months of continuous treatment is considered an adequate period for determining the efficacy of megestrol acetate.
6. Leuprolide (Lupron), goserelin acetate (Zoladex)
   Nursing Considerations
   - Maintaining the prescribed dose and schedule is very important.
   - Before administration, review with the patient the side effects of the drug. Tell the patient that symptoms may worsen in the first few weeks of therapy.
7. Bicalutamide (Casodex)
   Nursing Considerations
   - Bicalutamide interacts with dicumarol and warfarin. Monitor the patient carefully if he or she is taking flutamide and one of these agents.
8. Flutamide (Eulexin)
   Nursing Considerations
   - Flutamide interacts with warfarin. Monitor the patient carefully if he or she is taking flutamide and warfarin.

J. Nitrosoureas

Medication Names

1. Carmustine (BCNU)
   Nursing Considerations
   - Carmustine crosses the blood-brain barrier.
   - Nadir occurs 4-6 weeks after therapy starts.
   - Because of delayed toxicity, successive treatments usually are

given no more frequently than once every 6-8 weeks.
- Rapid infusion may cause burning along the vein and flushing of the skin.
- Long-term therapy can result in irreversible pulmonary fibrosis, which may present as an insidious cough and dyspnea or sudden respiratory failure.

2. Lomustine (CCNU)
   Nursing Considerations
   - Lomustine crosses the blood-brain barrier.
   - Because of delayed myelosuppression, do not repeat the dose more than once every 6 weeks.
3. Streptozocin (Zanosar) Not used in pediatrics.
   Nursing Considerations
   - Nephrotoxicity may be dose limiting.
   - This drug may alter glucose metabolism in some patients.
   - Rapid infusion may cause burning along the vein.

Table 5. Biologic Agents

A. Adoptive Immunotherapy (such as lymphokine-activated killer [LAK] cells, tumor-infiltrating lymphocytes [TILs])
   - Do not filter cells.
   - Agitate agent gently to avoid clumping.
   - Administer concurrently with interleukin-2 (IL-2).

B. Hematopoietic Growth Factors
   1. Erythropoietin
      - Do not shake product.
      - Do not freeze product.
      - Keep refrigerated.
      - Half-life: 4-13 hr.
      - Stop treatment if hematocrit (Hct) > 40% and resume at 75% of dose when Hct is 36%.
      - Expect increase in hemoglobin (Hgb) or Hct in 2-4 weeks.
      - Check Hct regularly.
   2. Granulocyte-Colony Stimulating Factor (G-CSF)
      - May be diluted in 5% dextrose.
      - Concentrations $\leq$ 15 mcg/ml require human serum albumin.
      - Do not dilute with saline.
      - Minimum concentration is 5 mcg/ml.
      - Refrigerate; do not freeze.
      - Avoid shaking G-CSF.
      - Administer when drug is at room temperature.
      - Discard if left out > 6 hr.
      - Refer to specific protocol and brochure in regard to this investigational drug.
      - Considerations vary with product source.
   3. Granulocyte Macrophage-Colony Stimulating Factor (GM-CSF)
      - Preservative-free lyophilized powder.
      - Dilute with normal saline.
      - For concentration $\leq$ 10 mcg/ml: Add human serum albumin

before GM-CSF, to prevent absorption of drug in IV container and tubing.
- Do not mix with dextrose.
- Do not filter agent.
- Refrigerate the drug.
- Do not freeze the drug.
- Discard unused vial after 6 hr.

4. Macrophage-Colony Stimulating Factor (M-CSF)
   - Refer to specific protocol and brochure in regard to this investigational drug.
   - Considerations vary with product source.
5. Interleukin 11 (IL-11)
   - Lyophilized powder.
   - Do not shake product.
   - Do not freeze product.
   - Use within 3 hr. of reconstitution when stored at 2Â°-8Â°C or at room temperature.
   - May exacerbate symptoms of congestive heart failure.

C. Interferons

0. Interferon Alfa (IFN-alpha)

Roferon-A (interferon alfa-2a)

- Available as solution and lyophilized powder; a recombinant product.
- Refrigerate product.
- Stable for 30 days after reconstitution if stored at 2Â°-8Â°C.
- Do not freeze product.
- Do not shake product.

Intron-A (interferon alfa-2b)

- Available as a multidose pen; a recombinant product.
- Refrigerate product.
- Stable for 30 days after reconstitution if stored at 2Â°-8Â° C.

Pegasys (pegylated interferon)

- Refer to specific protocol and brochure in regard to this investigational drug.

Alferon N (interferon alfa-n3)

- Supernatant from human white blood cells.
- Refrigerate product.
- Stability is marked on each vial.

Infergen (interferon alfacon-1)

- Refrigerate product.
- Do not freeze product.

- Avoid shaking the product and exposing it to direct light.

1. Interferon Beta (IFN-beta)

Avonex (interferon beta-1a)

- Lyophilized powder for injection; single-use vials.
- Refrigerate product at 2Â°-8Â°C.
- Use within 6 hr. of reconstitution.
- Do not freeze product.

Betaseron (interferon beta-1b)

- Lyophilized powder for injection; single-use vials.
- Refrigerate product at 2Â°-8Â°C.
- Use within 6 hr. of reconstitution.
- Do not freeze product.

2. Interferon Gamma (IFN-gamma)

Actimmune (interferon gamma-1b)

- 100 mcg = 3 million IU.
- Recombinant product; single-use vial.
- Do not freeze product.
- Do not shake product.
- Refrigerate product at 2Â°-8Â°C.
- Discard vials stored at room temperature for > 12 hr.

D. Interleukins

0. Interleukin-1 (IL-1)
    - Refer to specific protocol and brochure in regard to this investigational drug.
    - Use depends on the source of product.
1. Interleukin-2 (IL-2)
    - Lyophilized cake.
    - Do not use if patient has CNS metastasis or seizure disorder.
    - Do not use with an in-line filter.
    - Do not mix with normal saline or bacteriostatic water.
    - Do not mix with other medications.
    - Requires albumin at low concentration:
        - 5-60 mcg/ml: Mix in 0.1% human serum albumin.
        - 60-100 mcg/ml: Do not use this concentration.
        - 100 mcg/ml: Do not use albumin; dilution with albumin can alter pharmacology.
2. Interleukin-3 (IL-3)
    - Refer to specific protocol and brochure in regard to this investigational drug.
    - Use depends on source of product.
3. Interleukin-4 (IL-4)
    - Refer to specific protocol and brochure in regard to this investigational drug.
    - Use depends on source of product.
    - Dilution is limited to 20 mcg/1 ml for dose preparation.

- No antibacterial preservative is added.

4. Interleukin-6 (IL-6)
    - Refer to specific protocol and brochure in regard to this investigational drug.
    - Use depends on source of product.
5. Interleukin-12 (IL-12)
    - Refer to specific protocol and brochure in regard to this investigational drug.
    - Use depends on source of product.

E. Levamisole (Ergamisol)
- Increases phenytoin plasma levels.
- Store at room temperature.
- Protect from moisture.

F. Monoclonal Antibodies

0. OncoScint
    - Single use only
1. ProstaScint (capromab pendetide)
    - Single use only
2. Herceptin (trastuzumab)
    - Do not administer by IV push or bolus.
    - Do not freeze reconstituted product.
    - Stable at 2Â°-8Â°C before reconstitution; stable for 28 days thereafter.
    - Cardiac assessment required pretreatment.
3. Rituxan (rituximab)
    - Do not administer agent via IV push or bolus.
    - Stable at 2Â°-8Â°C for 24 hr. (an additional 12 hr. at room temperature)
    - Do not shake agent.
4. Mylotarg (gemtuzumab ozogamicin)
    - Do not administer agent via IV push or bolus.
    - Refrigerate at 2Â°-8Â°C.
    - Protect agent from light.
    - Use 1.2-micron terminal filter for administration.
    - Because of potential for allergic reactions, keep emergency drugs at bedside. Potential for allergic reaction increases with use of pure mouse (murine) monoclonal antibodies. Reactions occur less frequently with use of chimeric (mouse-human) and humanized monoclonal antibodies.
    - Potential cardiac toxicity.
    - Infusion-related reaction symptoms occur 30-120 min. after infusion starts.

G. Fusion protein (denileukin diftitox)
- Bring agent to room temperature before preparing it.
- Thaw agent at 2Â°-8Â°C no more than 24 hr. or at room temperature for 1-2 hr.
- Do not shake agent.
- Do not refreeze drug.
- Do not administer drug while using an in-line filter.

H. Tumor Necrosis Factor
- Caution: Prior to use, determine need for human serum albumin in dilutions, to prevent adherence to IV tubing and containers.

- Pentoxifylline and ciprofloxacin have been shown to alter endogenous tumor necrosis factor production.
- Refer to specific protocol and brochure in regard to this investigational drug.
- Use depends on source of product.

I. Vaccines
- Refer to specific protocol and brochure in regard to this investigational drug.

J. Gene Therapy
- Refer to specific protocol and brochure in regard to this investigational drug.

Angiogenesis and antiangiogenic agents

At the time of the printing of this guideline, the United States Food and Drug Administration (FDA) has not approved any antiangiogenic agents for use in oncology. Table 6 of the original guideline document cites some of the antiangiogenic agents currently in clinical trials. Table 7 in the original guideline document presents a list of some of the side effects of antiangiogenic agents. Always review clinical research protocol before administering an antiangiogenic agent. Know the side effects, interventions, and diagnostic studies that apply to the agent you will use.

Types of infusion for cytotoxic agents

See also the section below "Administration of cytotoxic agents." See Table 10 in the original guideline document, which cites the pros and cons of various administration practices. For pediatric patients, all chemotherapy (except that given intravenous push [IVP]) should be administered using a volumetric pump.

A. Piggyback, or short-term, infusion
1. Do not pinch the intravenous (IV) catheter to determine blood return and patency. Pinching causes a dramatic change in pressure that may rupture a vein. To check for blood return and IV patency:
    a. Use a suction check: Gently aspirate the line, using a syringe at the y-site closest to the patient while clamping or pinching off fluid from the bag.
    b. Use a gravity check: Remove the bag and tubing from the administration control device (the pump) and gently lower it to a point below the patient´s IV site.
2. Insert the connecting tubing into the appropriate primary tubing y-site; follow the drug manufacturer´s guidelines. (Some manufacturers recommend connecting at the highest y-site; others, at the lowest.) Use a Luer-lock connection or some other locking device to prevent disconnection.
3. Initiate flow rate in accordance with the physician´s orders or adjust the rate to administer the cytotoxic agent over a specified time.
4. If administering a vesicant in a peripheral vein:
    a. Administer the agent in a method that will decrease pressure on veins. For this reason, avoid the use of IV pumps.

b. Monitor the patient frequently for extravasation during the infusion--ideally, every 5 min.
c. Avoid hanging vesicant agents for extended periods, if possible.

5. Upon completion of the infusion, check for vein patency; use a sterile, noncytotoxic IV solution to flush the line.

B. Continuous, or long-term, infusion

1. Check for blood return and IV patency; see guidelines for piggyback infusion.
2. Connect the chemotherapeutic agent directly to the IV catheter or as a secondary infusion through a compatible maintenance solution.
3. Secure the connection site by using a Luer-lock connection or some other locking device.
4. Monitor the IV site throughout the infusion according to institution policy and procedure.
5. Check for blood return periodically during the infusion, according to institution policy and procedure.
6. If administering a vesicant:
    a. Do not use a peripheral IV for continuous vesicant administration.
    b. Use a central venous access catheter (CVC) or implanted access device to administer any vesicant infusion for longer than 30-60 min.
    c. Check for blood return and patency periodically during infusion, according to institution policy and procedure.
7. Upon completion of the infusion, check for vein patency; use sterile, noncytotoxic IV solution to flush the line.

C. IV push: Use the push-pull technique to administer a vesicant to children: Push a very small amount, pull back on the syringe to obtain a blood return, and then push a small amount again; continue until the total amount has been administered.

1. Free-flow method.
    a. Check for IV patency by gently aspirating the line at the y-site closest to the patient.
    b. Allow IV solution to flow freely.
    c. Slowly administer the agent by means of an IV push, using a free-flowing flush solution. Unless otherwise indicated, administer the agent at 1-2 cubic centimeter (cc) per min. If administering a vesicant, gently aspirate the line every 2-3 cc to verify blood return.
    d. Upon completion of the infusion, check for vein patency; use sterile, noncytotoxic IV solution to flush the line.
2. Direct-push method: At some institutions, policy mandates that some cytotoxic agents be administered via direct push into the IV catheter or butterfly needle.
    a. Establish patent IV access; use a syringe filled with sterile IV solution to flush the newly accessed line.
    b. Verify blood return and venous patency by aspirating the line gently.
    c. Detach the flush syringe; while maintaining sterile technique, attach the syringe containing the cytotoxic agent. Minimize blood loss.

d. Slowly administer the agent; every 1-2 cc, monitor venous patency by using the syringe of cytotoxic agent to aspirate the line gently.
e. Upon completion of the infusion, disconnect the cytotoxic syringe. Attach a syringe containing fresh sterile flush solution; gently flush the catheter. Avoid blood loss; the blood will contain the cytotoxic agent.
f. Check for vein patency; use sterile noncytotoxic IV solution to flush the line. If necessary, cap the access device.

Administration of cytotoxic agents

See also "Types of infusion for cytotoxic agents," above. Table 11 in the original guideline document lists the routes of administration for antineoplastic agents. Refer to Access Device Guidelines: Recommendations for Nursing Practice and Education (Camp-Sorrell, 1996) for a complete discussion.

A. Peripheral IV access: If possible, use a new administration site for vesicants. Avoid using a site that is more than 24 hr. old; the older the site, the less the integrity of the vein.
    1. Existing IV site
        a. If the site is established, assess the insertion site. Look for signs of inflammation and infiltration, and consider the patient´s statements about comfort. Use another access site if you doubt the integrity of the IV site or line.
        b. Assess blood return and site patency.
        c. Administer cytotoxic therapy.
    2. New IV site
        a. In adults:
            1. Search for an appropriate site by assessing the patient´s arm carefully; follow institution guidelines and policies relating to IV starts. If possible, do not establish a site:
                - On hands, antecubital areas, or the inner aspect of the wrist.
                - That involves low-flow, fragile, tortuous veins
                - In extremity with altered venous return or lymphedema
            2. Distend veins by using a heat pack or asking the patient to dangle hand and arm over the side of the bed. Avoid tourniquet use, which could rupture veins. If necessary, use a blood pressure cuff inflated to 40-50 mmHg on the upper arm to distend veins for venipuncture.
            3. Access vein by using appropriate methods.
            4. Establish blood return and patency.
            5. Secure the new IV site appropriately, in a manner that allows a clear view of the site.
        b. In children: search for an appropriate site, following institution policies and the guidelines that follow.
            1. Do not use as an IV site the feet or dominant hand of an infant or toddler.

2. The veins of the scalp of a child less than 12 months old can be used as an IV site; however, do not use a scalp vein as an administration route for a vesicant.
3. Consider use of a pharmacologic intervention (e.g., an EMLA anesthetic disc, Numby Stuff dermal anesthesia) for pain during IV insertion.
4. Stabilization of an extremity may be necessary during insertion and thereafter.

B. CVCs: CVCs include percutaneous subclavian catheters, tunneled subclavian catheters, and peripherally inserted central catheters. (A midline catheter is considered a peripheral line because it ends in the middle of the upper arm.) An implanted port, though technically a CVC, is unique. Implanted ports will be addressed in section C. Note: Most CVCs require the use of syringes larger than 10 cc to minimize pressure (pounds per square inch [psi]) on delicate catheter walls. Follow manufacturer´s and institution guidelines carefully to avoid catheter rupture and extravasation. After CVC insertion and before administering the agent:
    1. Verify that the type of catheter and its placement are correct.
    2. Inspect exit site for evidence of leakage. Inspect ipsilateral chest for signs of venous thrombosis.
    3. Inspect exit site for evidence of erythema, swelling, drainage, etc.
    4. Aspirate the line to ensure blood return. If blood return is not evident:
        a. Flush the catheter with saline, gently using the push-pull method. Avoid use of syringes less than 3 cc in size.
        b. Reposition the patient as appropriate. Ask the patient to cough.
        c. Explain to the patient why delaying therapy is necessary. Though the patient may indicate that not obtaining a blood return from his or her catheter is common and tells you to proceed, do not administer cytotoxic therapy. Remember that extravasation of a cytotoxic agent may have serious consequences.
        d. Obtain a physician´s order for a declotting procedure; follow institution protocol.
        e. Before administering a cytotoxic agent, use x-rays or dye studies to confirm proper CVC placement.

C. Implanted ports: Implanted ports are available that allow venous access, peritoneal access, arterial access, and epidural access. Ascertain which type is being used. Some patients have more than one type.
    1. Assess initial line placement by using the results of x-ray or fluoroscopic dye studies.
    2. Choose a noncoring, 90-degree needle whose length is appropriate to the:
        a. Depth of the port
        b. Size of the patient (i.e., the amount of subcutaneous tissue or fat located above the port)
    3. Prepare the patient´s skin according to institution policy.
    4. Access the port, ensuring proper placement of the needle in the reservoir.
    5. Establish blood return and patency for venous or arterial ports. Blood return is not expected with epidural or peritoneal access devices.
    6. Inspect the needle insertion site for needle dislodgement, leakage of IV fluid, drainage, or edema.
    7. Examine the ipsilateral chest for venous thrombosis.

8. Apply an occlusive dressing to stabilize the needle. The dressing should be transparent, to allow a clear view of the insertion site. Experts disagree about other characteristics that are desirable.
9. Refer to Access Device Guidelines: Recommendations for Nursing Practice and Education (Camp-Sorrell, 1996).

Pretreatment

During pretreatment and treatment, document assessment and care by using nursing and chemotherapy flow sheets as specified by institution guidelines. Appendices 3 and 4 in the original guideline document provide example flow sheets.

A. Nursing assessment and review of orders
    1. Take a history and review systems
        a. Review recent treatment, including surgery, prior cytotoxic therapy, radiation, and biologic and hormonal therapy
        b. Document medical and surgical history
        c. Document allergy history
        d. Assess the psychosocial status of patient and family
        e. Note cultural issues and considerations
        f. Review systems to assess the effects of disease and side effects of previous therapy
        g. Assess the patient´s performance status by using a subjective performance scale: Karnofsky, Zubrod, Eastern Cooperative Oncology Group (ECOG), or Lansky
        h. Document the patient´s height and weight; compare current measurements to previous measurements
        i. Review previous and current lab values
        j. Review tumor type, grade, and stage
        k. Consult psychologists, social workers, and dietitians as needed throughout the treatment course. When caring for pediatric patients, consult child-life specialists
    2. Assess the education of patient and family
        a. Note primary language
        b. Assess level of understanding of therapy, disease, etc.
        c. Identify barriers to learning (literacy, anxiety, etc.)
        d. Note desired level of participation in decision making
        e. Determine preferred learning method or style
        f. Assess the patient´s level of understanding concerning the details of cytotoxic treatment:
            1. Drugs, side effects, and home management
            2. When to call a nurse or physician
            3. Follow-up labs and follow-up care
        g. Give family members necessary telephone numbers, including the numbers for:
            1. Nurse
            2. Physician
            3. Home infusion firm
            4. Inpatient unit, ambulatory clinic, and/or physician's office
B. Review of the treatment plan

1. Compare written orders to formal drug protocol or reference source; identify the therapy prescription and administration source. Recommendation in regard to caring for pediatric patients: Two chemotherapy-competent members of the care team should check the written orders; ensure that the drug, dose, time, route, and relevant test results were within normal limits for the patient; and document these points or any deviation from them in the medical record.
2. Review the patient´s actual height and weight, doublecheck the patient´s BSA (see section XXII in the original guideline document)
3. Recalculate the dose as ordered per body surface area (BSA) or mg/kg; check your result against the written order
4. Verify that the dose is appropriate for the patient and treatment plan. In case of deviation, consult a physician or pharmacist.
5. Review drugs for vesicant or irritant potential; ensure that an extravasation kit is readily available
6. Identify drug side effects and toxicities. Determine if orders mandate premedication, and evaluate continuing side-effect management for appropriateness. Before cytotoxic therapies are administered, consult a physician or pharmacist if additional or different medications, routes, doses, times, etc. are required for optimal patient management.
7. If consent is required for the drug(s) to be administered, verify that written and/or verbal patient or parental consent has been obtained
8. Assess the patient´s prior experience with cytotoxic therapy; assess the patient´s understanding of and willingness to proceed with cytotoxic therapy

Refer to the original guideline document for a discussion of safe-practice considerations for cytotoxic and biotherapeutic agents.

<u>Storage and labeling of chemotherapeutic agents</u>

A. On-unit
    1. Store chemotherapy drug containers in a location that permits appropriate temperature and safety regulation
    2. Label all drug containers to indicate the hazardous nature of their contents
    3. Provide instructions (e.g., Material Safety Data Sheets, or MSDSs) regarding what to do in the event of accidental exposure
    4. Check cytotoxic drug containers before taking them from the storage area, to ensure that packaging is intact
B. In the home: See Appendix 2 in the original guideline document
    1. Keep all supplies out of the reach of children and pets
    2. Place drugs to be stored in a home into containers that provide adequate protection from puncture or breakage
    3. Label containers to indicate the hazardous nature of their contents
    4. Provide instructions that say what to do in case a container is damaged
    5. Keep supplies in an area free of moisture and temperature extremes
    6. Provide spill kits and instructions about their use
    7. Give verbal and written instructions about handling and storing cytotoxic agents and waste

Mixing chemotherapeutic and biotherapeutic drugs

A. Chemotherapeutic drugs
    1. Prepare cytotoxic drugs, including oral drugs that must be compounded or crushed, in a biological safety cabinet (BSC). The BSC should:
        a. Provide vertical laminar airflow. Vertical airflow is important because it will carry contaminated air away from the BSC operator and out of the environment.
        b. Eliminate exhaust through a high-efficiency particulate air (HEPA) filter. Ideally, a BSC should be vented to the outside.
        c. Have a blower that operates continuously
        d. Be serviced according to the manufacturer´s recommendations and be recertified every six months
        e. Be located in a low-traffic area, to reduce interference with airflow
        f. Be used by individuals trained to employ techniques that reduce interference with airflow
    2. Wash hands before donning personal protective equipment (PPE)
    3. Wear appropriate PPE
    4. Place a sterile, plastic-backed absorbent pad on the work surface
    5. Maintain sterile technique during the preparation of parenteral drugs
    6. Use appropriate technique when opening ampules
        a. Clear fluid from the ampule neck
        b. Tilt the ampule away from yourself
        c. Wrap gauze or an alcohol pad around the neck of the ampule
        d. Break the ampule in the direction away from yourself
        e. Use a filtered needle to withdraw fluid
    7. When reconstituting drugs packaged in vials, avoid aerosolization, which results from pressure build-up, by using dispensing pins with venting devices whenever possible
    8. Use tubing and syringes with Luer-lock fittings
    9. Avoid overfilling syringes. A syringe that is too full may separate from the plunger end.
    10. Prime all tubing with nondrug fluid before adding cytotoxic drugs, preferably in a BSC
    11. Place on each container a label that says "Cytotoxic Drug"
    12. Wipe the outside of the container with moist gauze before placing the container in a sealable bag for transport
    13. Dispose of all material that has come into contact with a cytotoxic drug by placing the material into a waste container designated for cytotoxic waste
    14. Remove and discard PPE
    15. Wash your hands before leaving the work area
B. Biotherapeutic drugs
    1. If preparing a nonradiolabeled agent:
        a. In general, inject the diluent into the vial, toward the side of the vial instead of directly into the powder. Doing so prevents foaming. Foaming can denature the protein and so interfere with its viability and biologic activity.
        b. Gently swirl the reconstituted agent; never shake it. Shaking, like foaming, can denature the protein. Most reconstituted

products are colorless. Products that should not be colorless are noted as such in manufacturer´s literature.

2. A nuclear pharmacist prepares radiolabeled monoclonal antibodies for infusion. Note: Federal and state laws require that radiation-safety warning signs designate the areas in which radioisotopes are stored or used.

Treatment

A. Preparation for therapy
    1. Explain to the patient and family the procedures for administration of:
        a. Premedications
        b. Adjunct medications
        c. Hydration
        d. Cytotoxic therapies
        e. Medications for side-effect management
    2. Identify plan for antiemetic management, if indicated. Describe procedures regarding:
        a. Hydration
        b. Medication
        c. Intake and output assessment
        d. Electrolyte monitoring
    3. Have available:
        a. A chemotherapy spill kit
        b. Extravasation management information and antidotes, if applicable
        c. Emergency drugs and equipment, based on patient history, drugs, treatment plan. If the patient is a child, ensure that patient-specific dosing cards and pediatric emergency equipment are available.
    4. Prepare the therapeutic agent. Check the syringe, bag, or bottle against the original order to ensure compliance with the "five rights" of drug administration: right route, right dose, right drug, right time, right patient. If preparing a nonradiolabeled agent, follow the guidelines cited in section XVII, Safe-Practice Considerations, in the original guideline document. Radiolabeled monoclonal antibodies are prepared for infusion by a nuclear pharmacist.

B. Therapy administration: See Table 12 in the original guideline document, which provides tips about giving oral chemotherapy to children. Double-check everything to prevent medication and administration errors.
    1. Administer prehydration and premedications as ordered.
    2. See Table 13 in the original guideline document, which presents pediatric guidelines regarding maximum volumes of intramuscular injections. Use a volumetric pump to administer chemotherapy to pediatric patients.
    3. Check for blood return and intravenous patency. Review guidelines in "Types of Infusion for Cytotoxic Agents" above.
    4. Flush the line with noncytotoxic fluid.
    5. Place a plastic-backed drape under the connection and a gauze pad under the access site during administration, to catch possible droplets and avoid exposing the patient´s skin to the drug.

6. Administer the cytotoxic agent, following all applicable guidelines and institution policies.
7. While administering cytotoxic therapy, observe the patient for any signs or symptoms of imminent side effects, such as hypersensitivity reactions (see section XXII in the original guideline document, Immediately Evident Complications of Cytotoxic Therapy). For a pediatric patient with continuous infusions, monitor the IV site at least once every hour.

C. Postadministration
1. Discontinue the drug, keeping administration sets and containers intact whenever possible.
2. Continue to monitor the patient for hypersensitivity reactions and other side effects of cytotoxic therapy.
3. Use detergent and water to wash surfaces that came into contact with cytotoxic agents.
4. Discard all contact material and PPE in a cytotoxic waste container.
5. Wash your hands.

Immediate complications of cytotoxic therapy

See Table 14 in the original guideline document, which lists the vesicants and irritants often responsible for immediately evident complications. Vocabulary frequently used in this section includes:

Vesicant: Any agent that has the potential to cause blistering or tissue necrosis.

Irritant: Any agent that causes a local inflammatory reaction but does not cause tissue necrosis.

A. Extravasation
1. Collaborative management of extravasation:
    a. Extravasation involving a peripheral line: At the first sign of infiltration:
        1. Stop administration of vesicant and IV fluids.
        2. Open the extravasation kit (see Figure 9 in the original guideline document).
        3. Disconnect the IV from the IV catheter or butterfly tubing. Do not remove the IV catheter or butterfly.
        4. Attempt to aspirate the residual drug from the catheter or butterfly by using a small (1-3 cc) syringe.
        5. Notify the physician.
        6. Administer the appropriate antidote, if known. Your intent should be to "infiltrate the infiltrate" with an antidote.
            - To administer the antidote through the catheter: Instill the appropriate volume into the IV catheter, and discontinue the IV catheter; avoid putting excess pressure on the site. Then follow policy guidelines.
            - To administer the antidote subcutaneously: Discontinue the IV catheter; avoid putting excess pressure on the site. Use a 25-gauge needle to

inject the antidote into the subcutaneous tissue. Avoid Z-tracking. Apply heat or cold to the site, as appropriate.

7. Initiate appropriate nursing-management measures according to Table 14 in the original guideline document, and institution policies.
8. Instruct the patient to rest and elevate the site for 48 hr. and then to resume normal activity.
9. Photograph the extravasation site if institution policy requires that the site be photographed.
10. Evaluate the extent of extravasation and tissue damage. Refer the patient to a plastic surgeon, if appropriate.

b. Extravasation involving a central line: Extravasation in the upper torso or neck area may result in serious defects and require extensive reconstructive surgery. It is imperative that the nurse administer vesicant therapy into a central line of any type very carefully.
    1. Immediately discontinue chemotherapy and IV fluids if the patient reports changes in sensation, pain, burning or swelling at the CVC site or in the ipsilateral chest, if a change occurs, or if no blood returns.
    2. If the patient has an implanted port, assess the site for proper needle placement.
    3. If possible, aspirate the residual drug from the area of suspected infiltrate at the port pocket or at the exit site of the tunneled or percutaneous catheter.
        - If extravasation is a result of needle dislodgment in a port, leave the needle in place and attempt to aspirate the residual drug.
        - If aspiration is unsuccessful, remove the needle from the port and attempt to aspirate the drug subcutaneously, from the pocket and surrounding tissue.
    4. Administer the appropriate antidote, if applicable, and initiate the appropriate nursing-management measures (see Table 14 in the original guideline document).
        - If the antidote is administered through the IV, instill the appropriate amount, avoiding excess pressure on the site, and apply local cold or heat.
        - If the patient has an implanted port, remove the port needle after instilling the antidote. Inject the antidote into subcutaneous tissue as appropriate and apply local cold or heat.
    5. Collaborate with the physician regarding
        - The need for a radiographic flow study to determine the cause of extravasation
        - Future plans for IV access and patient management

2. Documentation of an extravasation episode: Follow documentation guidelines provided in Figure 10 in the original guideline document and/ or institution guidelines. See also section XXXIV in the original guideline document, Legal Issues Related to Cancer Therapy.
3. Follow-up guidelines

a. Monitor the site at 24 hr., one week, two weeks, and as necessary for pain, redness, swelling, ulceration, or necrosis, depending on the degree of tissue damage. Follow up with serial photographs if possible.
b. Consult a plastic surgeon if a large volume was extravasated, if the patient experiences severe pain after the initial injury, or if minimal healing is evident one to three weeks after the initial injury.

4. Patient and family education
   a. Before cytotoxic therapy, inform the patient and family that extravasation is a possibility.
   b. After therapy, instruct the patient and family about the importance of immediately reporting symptoms of any delayed reaction.
   c. If an extravasation episode occurs, provide written instructions related to the care of the extravasation site and other follow-up.

B. Hypersensitivity, flare reaction, and anaphylaxis
1. Clinical management of localized hypersensitivity and flare response
   a. Observe and evaluate symptoms (e.g., urticaria).
   b. Administer diphenhydramine and/or corticosteroids per physician´s order or according to protocol.
   c. Monitor vital signs at least every 15 min. for 1 hr. or as the patient´s condition requires.
   d. Avoid administering subsequent doses if a patient is considered sensitized to the drug. If the drug is considered critical to the treatment plan, premedication with antihistamines and/or corticosteroids may prevent a recurrent hypersensitivity reaction.
2. Clinical management of flare reaction
   a. If extravasation is suspected: Stop administering the drugs and follow extravasation guidelines.
   b. If extravasation is not suspected: Flush the vein with saline and watch for resolution of flare.
   c. If resolution does not occur, get a physician´s order to administer hydrocortisone. For adults, the dose is 25-50 mg IV followed by a saline flush. For children, the dose is 0.8-4.0 mg/kg/day followed by a saline flush.
   d. Once the flare reaction has resolved, slowly resume infusion of the drug.
   e. If the drug is to be readministered at a later date, consider premedication with antihistamines and/or corticosteroids. Slowing infusion rates may be helpful.
   f. Document the episode, including all treatment and the patient´s responses, according to institution policies.
3. Clinical manifestations of hypersensitivity response and anaphylaxis:
   a. Urticaria (hives)
   b. Localized or generalized itching
   c. Shortness of breath, with or without wheezing
   d. Uneasiness or agitation
   e. Periorbital or facial edema
   f. Lightheadedness or dizziness
   g. Tightness in the chest

h. Abdominal cramping or nausea
i. Chills
j. Hypotension

4. Preadministration guidelines: Implement the steps that follow to prevent hypersensitivity reactions.
    a. Obtain and record baseline vital signs.
    b. Review the patient´s allergy history.
    c. Administer premedications as ordered.
    d. Ensure that emergency equipment and medications are readily available. This is especially important if chemotherapy is administered in the patient´s home or in another setting for nonacute care.
    e. Obtain physician´s orders for emergency drug procedures before drug administration.
    f. Instruct the patient to report hypersensitivity symptoms.
    g. Review reports of hypersensitivity before each treatment; hypersensitivity reactions can occur with a patient´s repeated exposure to a drug.
    h. Perform a scratch test or intradermal skin test, or administer a test dose before administering the initial dose of the drug to a patient who has a high likelihood of a hypersensitivity reaction.
        1. Observe the patient for any local or systemic reaction, which can occur 1 hr. or more after the test is performed. If no sign of hypersensitivity is evident, proceed with the initial dosing.
        2. When administering an IV-bolus drug that is associated with hypersensitivity, infuse the drug slowly and continue to observe the patient for signs and symptoms of hypersensitivity.
    i. Consider medication desensitization with the physician present.
        1. Premedicate with antihistamines and/or corticosteroids.
        2. Dilute the drug with additional solution.
        3. Increase infusion time.
        4. Discuss with the physician the possibility of substituting a similar drug.
    j. Emergency management of anaphylaxis: The need for emergency management usually arises within 15 min. of administration. Immediate action is imperative.
        1. Stop chemotherapy infusion immediately.
        2. Stay with the patient. Another staff member should notify the physician and emergency team or, if outside a hospital setting, call the local emergency medical service.
        3. Maintain an IV line with normal saline or another appropriate solution.
        4. Place the patient in a supine position.
        5. Monitor vital signs every 2 min. until the patient is stable, then every 5 min. for 30 min., then every 15 min.
        6. Maintain airway, assessing the patient for increasing edema of the respiratory tract. Administer oxygen if needed. Anticipate the need for cardiopulmonary resuscitation (CPR).

7. Administer emergency medications (see Table 17 in the original guideline document).
8. Provide emotional support to the patient and family.
9. Document all treatment and the patient´s responses in the medical record.

Refer to the original guideline document for discussion of the following topics: radiation protection during biotherapy, radiation monitoring, transporting chemotherapeutic drugs, safe-handling considerations during administration, handling a patient´s body fluids, handling a patient´s linens after chemotherapy, disposal of cytotoxic materials, procedures following acute accidental cytotoxic exposure, and spill management.

Side Effects--Principles of Management and Patient Education

Refer to the original guideline document for general principles of cytotoxic therapy. In regard to the side effects of biotherapy and their management, see Table 20 in the original guideline document, and Table 21 below.

Guidelines for discussing side effects with patients

1. Ascertain the patient´s knowledge level and expectations before discussing side effects. A patient´s experience or the experience of a relative or friend may cause the patient to have misconceptions about therapy. These misconceptions may even prevent the patient from undergoing treatment. Tailor teaching to the patient. If appropriate, stress the improvements that have been made in supportive care in the last 10 years, along with the reduction in side effects.
2. Educate the patient and family about treatment side effects--citing the importance of monitoring, identification, and intervention--without unduly frightening them.

Table 21. Nursing Management of General Side Effects of Biotherapy

A. Cardiovascular
    1. Hypotension

        Monitoring Parameter(s)

        - Monitor blood pressure as needed based on clinical status.
        - Monitor fluids and electrolytes for imbalance.
        - Assess central venous pressure if appropriate.
        - Assess syncope, dizziness, weakness, and color.
        - Assess neurologic, renal, cardiovascular, and pulmonary status.

        Intervention(s)

        - Teach patient to:
            - Report signs of dizziness, light-headedness

- Change positions gradually
- Avoid hot showers and excessive heat

- If moderate to severe hypotension occurs, keep the bed flat or in a modified Trendelenburg position.
- Administer IV fluids judiciously.
- Vasopressors may be used according to institution guidelines to maintain renal perfusion and blood pressure.
- Per protocol, hold or discontinue dose administration.

Comment(s)

- Interleukin-2: Use IV fluid boluses carefully. They may result in pulmonary edema.
- The idiosyncratic first-dose reaction with GM-CSF may be accompanied by transient flushing, tachycardia, and hypoxia.
- Slow initial infusions of monoclonal antibodies may help prevent hypotensive reactions.

2. Arrhythmia

Monitoring Parameter(s)

- Continuous telemetry is needed in cases of severe hypotension or in the presence of arrhythmia.
- Assess rhythm, vital signs, and heart sounds on a regular basis.
- Assess the patient for chest pain or palpitations.
- Assess cardiac isoenzymes as indicated.

Intervention(s)

- Treat arrhythmias with appropriate medications as ordered.
- Explain all interventions to patient and family.

Comment(s)

- Interleukin-2, interferons, and interleukin 11: Dose may need to be held or discontinued.

3. Capillary leak syndrome

Monitoring Parameter(s)

- Monitor:
  - Intake and output, and weight (daily)
  - Abdominal girth
  - Electrolytes
  - Oxygen saturation
- Position patient to maximize ventilation and perfusion.
- Provide comfort measures.
- Provide oxygen therapy.
- Use vasopressors to maintain blood pressure.

Intervention(s)

- Interstitial fluid mobilizes 24-48 hr. after discontinuation of interleukin-2.
- Ensure that complaints of chest pain are medically evaluated to determine etiology.

Comment(s)

- Interleukin-2, tumor necrosis factor (TNF), or fusion protein: Dose may need to be held or discontinued.

B. Cutaneous Effects

1. Dry desquamation

Monitoring Parameter(s)

- Assess skin color, pigmentation, texture, turgor, vascularity, skin integrity, presence of lesions, eruptions, petechiae, purpura, edema, and pruritus.
- Assess injection site to ascertain dermatologic effect or infectious etiology.

Intervention(s)

- Use mild soaps and rinse thoroughly.
- Avoid lotions with alcohol, perfumes, and chemicals.
- Use emollients and creams generously.
- Avoid steroid creams.

Comment(s)

- Antihistamines may be contraindicated in certain regimens.

2. Pruritus

Intervention(s)

- Antihistamines may provide relief.
- Adjust room humidity to 30%-40%.
- Ensure that the patient:
  - Avoids frequent hot showers and baths
  - Uses mild soaps and rinses thoroughly
  - Keeps nails short
- Cleanse ulcerations frequently and expose them to air.
- Apply cool towels.

Comment(s)

- Antihistamines may be contraindicated in certain regimens.

3. Transient flushing/Flare reaction

Monitoring Parameter(s)

- Assess patient for signs and symptoms of dermatologic effects: skin color, pigmentation, texture, turgor, vascularity, skin integrity, presence of lesions, eruptions, petechiae, purpura, edema, and pruritus.
- Assess injection site to ascertain dermatologic effect or infectious etiology.

Intervention(s)

- For interleukin-2 and -12, CSFs, TNF, GM-CSF, vaccines
  - Rotate injection sites.
  - Split high-volume doses into two syringes for two separate injections.
  - Ask physician whether to apply ice or heat to site pre- and postinjection.
  - Premedicate patient with diphenhydramine if pruritus develops.

4. Alopecia

Intervention(s)

- Before treatment, alert the patient to the potential for alopecia.

C. Flu-Like Symptoms

1. Fever

Monitoring Parameter(s)

- Monitor temperature pattern.
- If fever is unresponsive to acetaminophen, assess patient for infectious etiology.

Intervention(s)

- Premedicate with acetaminophen or NSAIDs; 24-hr. administration may be needed.
- Maintain adequate fluid intake.
- Regulate environmental temperature.
- Take measures to decrease fever:
  - Sponge bath
  - Removal of extra clothing and blankets
  - Use of cooling blanket as needed

Comment(s)

- Route, dose, and frequency of agent will determine temperature pattern and intensity.
- Fever associated with interferon administration diminishes in intensity with continued treatments.

- A sharp elevation in temperature after an afebrile period without changes in drug administration, or fever unresponsive to acetaminophen, may indicate infection.

2. Chills or rigors (shaking chills)

   Monitoring Parameter(s)

   - Monitor temperature and comfort.

   Intervention(s)

   - Administer opiates to relieve rigors (IV meperidine, IV morphine, sublingual hydromorphine).
   - Antipyretic premedications may be used with some treatment regimens.
   - Minimize chills/rigors by using:
     - Heating pads
     - Hot-water bottles
     - Extra blankets

   Comment(s)

   - Opiate administration may potentiate decreased blood pressure.
   - Predictable pattern occurs with rise in temperature.

3. Myalgia or arthralgia

   Monitoring Parameter(s)

   - Assess patient for presence of myalgia or arthralgia

   Intervention(s)

   - Administer NSAIDs.
   - Administer oral analgesics.
   - Provide comfort measures.
   - Provide local moist heat.

4. Headache

   Intervention(s)

   - Provide analgesia
   - Maintain a quiet, dark room

5. Malaise

   Monitoring Parameter(s)

   - Assess objective and subjective indicators of patient´s activity status.

Intervention(s)

- Employ energy-conservation strategies.

6. Fatigue

Monitoring Parameter(s)

- Perform subjective and objective assessment of patient´s ability to participate in activities of daily living (performance status).
- Monitor for presence and degree of immobility, sensory deprivation, and depression.
- Monitor for physical signs or symptoms of concurrent health problem(s) (e.g., anemia).

Intervention(s)

- Help the patient employ energy-conservation strategies, including priority setting.
- Help the patient maintain an appropriate level of physical activity.
- Provide optimal fluid intake and nutrition.
- Control pain.
- Correct anemia if it is present.

Comment(s)

- Medications used to alleviate concurrent symptoms (e.g., antiemetics, narcotics) may compound fatigue.

D. Gastrointestinal

1. Nausea and/or vomiting

Monitoring Parameter(s)

- Assess patient for nausea.
- Monitor frequency and amount of nausea or vomiting.

Intervention(s)

- Provide:
  - Routine antiemetic coverage
  - Frequent mouth care
- Serve food at room temperature.
- Modify diet as needed to clear liquid or frequent light meals.
- Minimize triggering stimuli in the environment.
- Offer relaxation or distraction therapy.
- Obtain nutrition consult.

Comment(s)

- Steroids may be contraindicated because of their immunosuppressive effects.
- Phenothiazines are effective.
- Metoclopramide may potentiate diarrhea.
- For denileukin diftitox: Nausea and vomiting are dose-limiting toxicities.

2. Anorexia

Monitoring Parameter(s)

- Monitor:
  - Weight loss or gain
  - Calorie count; maintain intake
  - Lab indices of visceral protein (e.g. albumin)
  - For evidence of fat and muscle wasting
- Determine calorie and protein needs in collaboration with a dietitian.

Intervention(s)

- Encourage the patient to:
  - Eat small high-protein, high-calorie meals frequently
  - Increase daily protein intake
  - Avoid filling or gas-forming food
- Teach the patient to eat slowly.
- Obtain dietary evaluation for the patient in regard to protein depletion and weight loss.

Comment(s)

- To the patient, food may seem to have less taste or to taste salty, bitter, or metallic. Some patients develop intolerance of sweets.
- For interferons: Anorexia may be dose limiting.
- Fatigue or depression may contribute to anorexic symptoms.
- Anorexia induced by gemtuzumab ozogamicin may be caused by metabolites from the calicheamicin derivative.

3. Diarrhea (more than three stools per day)

Monitoring Parameter(s)

- Assess:
  - Number of stools per day
  - For presence of fecal impaction
  - Bowel sounds
  - Hydration and electrolyte status
- Monitor:
  - Input and output
  - Frequency, duration, character, and amount of diarrhea
- Administer replacement fluids as ordered.

Intervention(s)

- Administer antidiarrheal medications as ordered.
- Provide perineal care to prevent skin breakdown.

Comment(s)

- Interferons used in conjunction with antimetabolites may increase diarrhea.
- Trastuzumab used in combination with chemotherapy increases the severity of diarrhea.
- Diarrhea caused by biotherapy is more chronic but less severe than diarrhea caused by chemotherapy.

4. Stomatitis

Monitoring Parameter(s)

- Assess oral cavity frequently.

Intervention(s)

- Provide:
  - Frequent oral hygiene
  - Topical analgesics
  - High-protein diet
- Increase fluid intake.
- Avoid trauma to mucous membranes.

Comment(s)

- Interferons may activate herpes simplex virus.

E. Hematologic

1. Neutropenia, thrombocytopenia, anemia

Monitoring Parameter(s)

- Monitor complete blood count, differential, and platelet count.
- Assess patient for signs and symptoms: infection, bleeding, and anemia.

Intervention(s)

- Initiate precautions against:
  - Bleeding
  - Neutropenia
- Administer blood or blood products as ordered.

Comment(s)

- Condition reverses rapidly upon cessation of therapy.

F. Neurologic Effects

1. Confusion or hallucinations/ Depression/ Anxiety/ Lethargy or somnolence/ Headache/ Decreased concentration/ Insomnia/ Irritability, mood changes/ Peripheral neuropathy/ Dizziness/ Paresthesia/ Hallucinations/ Seizures or coma

Monitoring Parameter(s)

- Assess mental status, cranial nerves, neuromotor function, and reflexes.
- Assess normal coping strategies.
- Obtain baseline assessment (should include contributing factors [e.g., age, performance status, psychological history, underlying disease process]).
- Perform ongoing and routine neurologic assessments.

Intervention(s)

- Provide:
  - Patient and family education regarding potential neurologic side effects
  - Memory prompts for orientation in regard to time, date, location
- Take patient safety measures.
- Encourage:
  - Patient and family expression of fears and concerns
  - Regular sleep routines
- Caution the patient against drinking alcohol.
- Evaluate providing treatment of the following types:
  - Behavioral
  - Pharmacologic
  - Antidepressant
  - Opioid antagonist
  - Psychostimulant

Comment(s)

- Differential diagnosis may include intensive care unit (ICU) psychosis.
- At increased risk: the elderly, patients with a psychiatric history. For these patients, treatment (particularly with interleukin-2, interferons) may be contraindicated.
- Interleukin-2: Concurrent administration of psychotropic drugs (e.g., narcotics, analgesics, antiemetics, antihistamines) may exacerbate neurologic toxicities.
- Neurologic toxicities are common reasons for dose reduction or termination.
- When a drug is discontinued, the severity of the toxicity may increase before improvement occurs.
- The patient may not regain baseline neurologic status for 2-4 weeks after treatment ends.

G. Pulmonary

1. Respiratory symptoms: Dyspnea, Pulmonary Edema, Acute Respiratory Distress Syndrome (ARDS), Pleural Effusion

Monitoring Parameter(s)

- Monitor:
  - Lung sounds at least every 4 hr.
  - Rate, rhythm, and depth of respiration
  - For behavior changes
  - Intake and output
  - Oxygen saturation
- Assess:
  - Use of accessory muscles and presence of retractions
  - Symmetry of chest
  - Cough (color, amount of sputum)
  - Chest or back pain
  - Skin color
  - Level of consciousness

Intervention(s)

- Position patient so he or she is comfortable.
- Provide:
  - Oxygen per nasal cannula or face mask, per order
  - Comfort measures
  - Effective analgesia
  - Anticipatory teaching regarding ICU transfer; intubation may be necessary
- Limit patient´s activity.
- Elevate head of bed.
- Administer diuretics and bronchodilators as ordered.
- Take aspiration precautions as indicated.
- Promote mucus clearance.

Comment(s)

- Use assessment techniques and intervention outcomes to prevent severe respiratory distress and need for ventilatory support.
- Interleukin-2 dose may be held or discontinued.

H. Renal

1. Elevated creatinine, blood urea nitrogen, and uric acid

Monitoring Parameter(s)

- Monitor:
  - Daily lab results (especially creatinine, blood urea nitrogen, chemistries)
  - Intake and output
  - Specific gravity and pH of urine

- Vital signs
- Assess:
  - Proteinuria
  - Hematuria
  - Flank pain

Intervention(s)

- Increase oral intake of fluids.
- Hydrate the patient by using IV fluids or colloids.
- Administer diuretics if patient´s blood pressure is stable.
- Alter diet as appropriate.
- Encourage the patient to void frequently.

Comment(s)

- For patients receiving high-dose interleukin-2: maintain hydration at a minimal level because of the exacerbation caused by capillary leak syndrome.
- Use diuretics as indicated to "pull" excess accumulated fluid.

2. Oliguria

Monitoring Parameter(s)

- Monitor intake and output every 4 hr. or per clinical status.

Intervention(s)

- Administer low-dose dopamine (2-5 mcg/kg/min.) to assist in maintaining renal perfusion.
- Until output resumes, holding interleukin-2 dose may be necessary.

Comment(s)

- Dopamine is titrated based on vital signs and urine output.
- Low urine output is consistent with high-dose treatment regardless of interventions.

Myelosuppression

A. Neutropenia:

1. Assessment: Use laboratory data to assess the presence of neutropenia by calculating absolute neutrophil count (ANC). It is important to note that neutropenia can occur when the total white blood cell (WBC) is within a normal range (4,000-10,000/ mm^3). Consequently, qualitating the ANC is essential to achieving a correct assessment of neutrophil status. To calculate ANC:
   a. Obtain complete WBC, including differential.

b. Add neutrophils (polys [segs] and bands).
c. Convert sum to percentage
d. Multiply total WBC by total neutrophil percentage (polys + bands).

ANC calculation example: WBC = 1,600, polys = 48, bands = 5.

- Add polys and bands: 48 + 5 = 53.
- Convert sum to percentage: 53 Ã· 100 = 0.53 = 53%.
- Multiple WBC by percentage to find ANC: 1,600 x 0.53 = 848.

2. Collaborative management
   a. Prevention
      1. Protective isolation has been found to have no effect on the host´s endogenous flora and no impact on organisms transmitted by water or food. For this reason, precautions regarding various fresh fruits and vegetables remain controversial.
      2. Treatment with granulocyte-colony stimulating factor (G-CSF): The development of colony stimulating factors (CSFs) has had an enormous impact on the incidence of infection related to chemotherapy. At the date the guideline was developed, only G-CSF is FDA-approved as a preventive for chemotherapy-induced neutropenia. Granulocyte macrophage colony-stimulating factor (GM-CSF) is FDA-approved only for acceleration of bone marrow recovery (recovery of myeloid cells) after autologous or allogeneic bone marrow transplant (BMT). Both G-CSF and GM-CSF have FDA indications for use following induction chemotherapy in acute myelogenous leukemia, mobilization of peripheral blood progenitor cells (PBPCs), following transplantation of autologous PBPCs; and in BMT failure or engraftment delay. When CSFs should be initiated and at what point they should be discontinued is a matter of debate. The manufacturer recommends initiation no earlier than 24 hr. following chemotherapy and continuing daily until an ANC > 10,000/mm^3 is achieved. Note: Insurance coverage for treatment with all colony stimulating factors varies widely.
      3. Prevent trauma to the patient´s skin and mucous membranes.
         - Avoid the use of catheters, enemas, nasogastric (NG) tubes, and rectal thermometers.
         - Prevent pressure sores and constipation.
         - Cleanse and protect wounds as directed
         - Use only an electric razor to shave the patient.
      4. Teach patients neutropenia protective measures that they can employ.
         - Wash hands frequently.
         - Bathe daily.

- Protect skin from cuts and burns.
- Wear gloves when working in the garden.
- Care for the mouth before and after meals.
- Care for the perineal area after voiding and bowel movements: Measures may include cleansing with povidone iodine or fresh-water sitz baths.
- Use only an electric razor to shave unwanted body hair.
- Use a water-soluble lubricant (e.g., Astroglide lubricant) during sexual intercourse, and practice effective postcoital hygiene. Patients with severe neutropenia should not have sexual intercourse.
- Exercise daily (e.g., walking, running) as tolerated.
- Do coughing and deep-breathing exercises (e.g., exercises that use an incentive spirometer) to decrease pulmonary stasis, thereby decreasing the potential for infection.
- Avoid people with colds or contagious illnesses (e.g., chicken pox, herpes zoster, influenza).
- Avoid people who were recently vaccinated with a live vaccine.
- Do not share food utensils.
- Do not provide direct care for pets.
- Avoid animal excreta; assign litterbox and birdcage cleaning to someone else.
- Do not use tampons, enemas, or rectal suppositories.
- Do not receive live vaccinations (e.g., a vaccination for polio).

b. Management of neutropenic fever: Data regarding the efficacy of CSFs after a patient is diagnosed with febrile neutropenia are inconclusive. To manage neutropenic fever, the clinician should:
    0. Culture urine, all lumens of CVCs, peripheral blood, and other suspected sources of infection. When dealing with pediatric patients, a culture is indicated only if the patient does not have a CVC.
    1. Perform a physical assessment in an attempt to identify the source of infection.
    2. For all adults, obtain a chest x-ray. For children, obtain a chest x-ray only if the patient´s condition warrants.
    3. Administer empiric antibiotics, which should include coverage for gram-positive and gram-negative organisms as ordered until organism source is identified
    4. Monitor blood culture reports daily

3. Patient and family education
    a. Teach the patient and significant others to report:
        0. Temperature elevation $\geq$ 38Â°C (100.4Â°F)
        1. Shaking chills (rigors)
        2. Dysuria
        3. Dyspnea
        4. Respiratory congestion or sputum production. Note: Children do not produce sputum.

5. Pain

b. Reinforce the need for meticulous hygiene.
c. Teach the patient (or parent) how to administer G-CSF or GM-CSF if applicable.

B. Anemia

1. Collaborative management

a. Identify the underlying cause of the anemia.
b. Implement iron supplementation only for patients with anemia related to iron deficiency.
c. Address symptoms related to hypoxia:

0. Encourage adult patients to rest to conserve energy. Children with anemia will set their own limits on activity. They may nap more often or not want to participate in favorite activities.
1. Administer oxygen if oxygen saturation is less than 90%.

d. Compare lab results with important lab indices: Table 24 in the original guideline document presents results that are considered in the normal range for healthy men and women. If a patient´s results are abnormal, take appropriate action.
e. Administer recombinant human (rHu) erythropoietin (EPO)-alfa as ordered. Note: The FDA has not approved the use of rHu EPO for children.

0. Patient selection: Hematocrit (Hct) of less than 30% or hemoglobin (Hgb) of less than 9 g/dl and one of the following:
    - Patient is receiving radiation and/or chemotherapy
    - Patient´s bone marrow is infiltrated by tumor
    - Patient has a myelodysplastic syndrome
    - Transferrin saturation is at least 20%
    - Serum ferritin level is > 100 ng/ml
1. Dosing criteria: refer to the original guideline document
2. Monitoring
    - After initiation of rHu EPO-alfa therapy, monitor Hct at least weekly until it reaches 30%.
    - Once a therapeutic dose has been established, monitor Hct at least monthly. Therapy should be discontinued when Hct is 36% or greater or when Hgb is $\geq$ 12 g/dl.
    - If Hct drops below 25%, Hgb drops below 8g/dl, or cardiopulmonary symptoms develop, administer 1-2 units packed RBCs over 2-3 hr.
        - If the patient has a history of hypersensitivity: Premedicate, 30 min. before transfusion, with acetaminophen 650 mg orally and diphenhydramine 25-50 mg orally or IV. Use a leukocyte filter during administration, or administer leukocyte-depleted packed RBCs.
        - If the patient is immunocompromised: Administer irradiated packed RBCs, using a leukocyte filter. One unit of packed

RBCs can raise Hct by 3% and Hgb by 1g/dl. Monitor tolerance to fluids: If the patient retains fluids, administer furosemide 10-40 mg IV, per physician´s order, after the first unit infuses. Repeat after 2-3 hr. if needed. Monitor for transfusion reaction.

2. Patient and family education
    a. Encourage the patient to rest to conserve energy.
    b. Encourage the patient to change positions slowly to prevent dizziness secondary to postural hypotension.
    c. Acknowledge patient´s reports of symptoms, such as fatigue, as real, even if stated in vague terminology.
    d. Discuss the potential for anemia and the signs and symptoms of anemia when teaching patients about the side effects of chemotherapy.
    e. Help patients and families develop mechanisms for managing persistent symptoms of anemia (e.g., fatigue, shortness of breath, decreased stamina).
    f. Provide instruction regarding the self-administration of EPO, including written materials, if applicable.
    g. Consult with a registered dietitian regarding an iron-rich diet for the patient and the relation between diet and RBC production.
    h. Teach patients and families about the hazards, risks, and benefits of blood transfusions.

C. Thrombocytopenia
1. Collaborative management
    a. Maintain and reinforce bleeding precautions when the platelet count is $\leq$ 50,000/mm^3.
    b. Decrease the patient´s activity to prevent injury (e.g., falls, bumping into objects). Children should not ride bicycles or skateboards, participate in contact sports, or engage in other activities that pose a high risk of injury.
    c. Maintain a safe environment (e.g., use nonskid rugs rather than rugs that could skid).
    d. Maintain the integrity of skin.
        0. Use electric versus straight-edged razors.
        1. Use an emery board versus metal file for nail care, or use metal nail clippers.
        2. Ensure that the patient knows to avoid wearing restrictive clothing (especially restrictive undergarments).
        3. Do not use tourniquets.
        4. Minimize invasive procedures, e.g., needlesticks, injections (especially intramuscular [IM] injections).
        5. Discourage all contact sports.
    e. Maintain integrity of mucous membranes.
        0. Encourage the patient to:
            - Blow his or her nose gently
            - Use a water-based lubricant before sexual intercourse

- Use only a soft toothbrush or sponge-tipped applicator, and rinse the mouth with a mild saltwater solution

1. Discourage the patient from:
    - Having dental care until platelets normalize
    - Using dental floss or oral irrigation tools
    - Having sexual intercourse if the platelet count is $\leq$ 50,000/mm^3
    - Using tampons
    - Having anal intercourse

f. Maintain the integrity of the genitourinary tract.
    0. Increase the patient´s hydration and avoid the use of indwelling catheters whenever possible. If catheterization becomes necessary, use only a small-lumen catheter and ample lubrication.
    1. Encourage the patient to drink more fluids; he or she should drink 2-3 liters per day.

g. Maintain the integrity of the GI tract.
    0. Encourage the patient to take steroids with milk or milk products, if steroids are ordered.
    1. Use prophylactic stool softeners to avoid constipation; avoid using enemas, suppositories, harsh laxatives, or rectal thermometers.

h. Maintain optimal nutrition status.
    0. Encourage consumption of protein-containing foods; protein is needed for megakaryocyte production.
    1. Encourage a soft diet that avoids foods that are thermally or chemically irritating.
    2. Discourage alcohol use.

i. Avoid all medications that have the potential to induce bleeding.

j. Administer appropriate medications and treatments.
    0. Administer platelets prophylactically to adults when the platelet count is 10,000-20,000/mm^3 or when the patient is symptomatic (bleeding), based on institution guidelines or protocol. (Patients with brain tumors usually receive platelet transfusions if the count drops below 50,000/mm^3.) The general rule of thumb is to hold transfusions until the platelet count drops to $\leq$ 10,000/mm^3. Prophylactic transfusions are not given routinely to children unless they have a large mass and there is a concern about bleeding into the tumor. For children, repeated exposure to donor-platelet antigens causes alloimmunization; the child will become refractory to transfusion treatment.
    1. Administer stool softeners or laxatives to avoid constipation.
    2. Consider administering IL 11, also known as oprelvekin, to minimize chemotherapy-induced thrombocytopenia. The FDA has approved IL 11 as a growth factor for megakaryocytes in nonmyeloid malignancies and nonmyeloblative chemotherapy regimens. IL 11 is presently not used in pediatrics.

- Be cautious when administering IL 11 to patients with a history of fluid retention, congestive heart (CHF), atrial arrhythmias, or coronary artery disease; patients, such as the elderly, who are at risk for developing any of the preceding symptoms; or patients who are heavily pretreated with anthracyclines.
- If IL 11 is ordered, administer the dosage subcutaneously on a daily basis at 50 micrograms (mcg) per kilogram per day, beginning 6-24 hr. after completion of chemotherapy. The manufacturer recommends that the drug be discontinued when the postnadir platelet count reaches 50,000/mm^3. Monitor patients closely (preferably daily) for dyspnea, pleural effusion, and edema. These side effects are thought to result from an increase in renal sodium retention and plasma volume expansion, which cause an increase in intravascular fluid.

2. Patient and Family Education
    a. Tell the patient and family to immediately notify the nurse or physician of symptoms of bleeding.
    b. Instruct the patient and family about the signs of transfusion reaction.
    c. Reassure the patient and family by discussing the fact that chemotherapy-related platelet disorder is generally short-lived. Share the prediction for nadir and outline the patient´s specific regimen.
    d. Reinforce the need to avoid injuries; list the activities the patient should avoid to prevent injury.
    e. Provide instruction regarding self-administration of IL 11, if applicable.
    f. Teach the patient and family interventions to manage bleeding.
    g. Provide healthcare providers´ names and telephone numbers, and ensure that the patient understands the need to notify contacts if he or she should experience:
        0. Bleeding from any body orifice
        1. New petechiae or bruising
        2. Change in level of consciousness (LOC)
    h. Provide a list of medications that may interfere with megakaryocyte production.

<u>GI and Mucosal Side Effects</u>

A. Nausea and Vomiting
1. Assessment: Determine the potential causes of nausea and vomiting.
    a. Physical causes: Tumor obstruction, constipation, increased intracranial pressure, uncontrolled pain.
    b. Metabolic causes: Hypercalcemia, uremia, increased creatinine.
    c. Psychological causes: Anxiety, fear, emotional distress.
2. Collaborative management--Pharmacologic actions: See Table 26 in the original guideline document. Choose antiemetics appropriate to the

antineoplastic agent and the dose administered. Administer antiemetics to cover the expected emetogenic period of the antineoplastic, considering duration and pattern of emesis. Note: Steroids are usually contraindicated for patients receiving biotherapy agents. Corticosteroids are not routinely used to control nausea and vomiting for pediatric patients with certain diseases (i.e., leukemia, brain tumor).

a. To manage acute nausea and vomiting:
    1. For patients at high risk: Use a combination of a $5HT_3$ antagonist plus a corticosteroid before chemotherapy.
    2. For patients at intermediate risk: Use a corticosteroid before chemotherapy.
    3. For patients at low risk: Do not routinely administer an antiemetic before chemotherapy.
    4. For patients who will undergo combination chemotherapy: Use an antiemetic appropriate to the chemotherapeutic agent presenting the greatest emetic risk.
    5. For patients undergoing multiple consecutive days of chemotherapy: Each day, use antiemetics appropriate to the risk category of the chemotherapy to be administered that day.
b. To manage delayed nausea and vomiting:
    1. For patients at high risk and being treated with cisplatin: Use a corticosteroid plus metoclopramide plus a $5HT_3$ antagonist. Metoclopramide is rarely used for pediatric patients.
    2. For patients at high risk who are not being treated with cisplatin: Use a prophylactic corticosteroid as a single agent, a prophylactic corticosteroid plus metoclopramide, or a prophylactic corticosteroid plus a $5HT_3$ antagonist. Metoclopramide is rarely used for pediatric patients.
    3. For patients at intermediate risk: Do not routinely use antiemetics for delayed emesis.
c. To manage anticipatory nausea and vomiting: Use the most active antiemetic regimens appropriate to the chemotherapy being given. Such regimens must be used with the initial chemotherapy rather than after assessment of the patient´s emetic response to less effective treatment.
d. To manage special nausea and vomiting problems:
    1. For patients undergoing high-dose chemotherapy: Use a $5HT_3$ antagonist plus a corticosteroid.
    2. For patients experiencing nausea and vomiting despite optimal prophylaxis in current or prior cycles: Ascertain that the best regimen is being given for the emetic setting; conduct a careful evaluation of risk, antiemetic, chemotherapy, tumor, and concurrent and medication factors; consider adding an antianxiety agent to the regimen; consider substituting a dopamine receptor antagonist, such as high-dose metoclopramide, for the $5HT_3$ antagonist (or add the dopamine antagonist to the

regimen). Metoclopramide is rarely used for pediatric patients.

3. Collaborative management--Psychosocial interventions
    a. Music therapy has been shown to significantly reduce the incidence of nausea and vomiting among patients who receive highly emetogenic chemotherapy. Music therapy is the controlled use of music to influence physiologic, psychologic, and emotional responses. Music therapy is often used with other techniques. It also decreases the perceptions of the degree of vomiting.
    b. Moderate aerobic exercise has been demonstrated to provide relief of nausea.
    c. Acupressure wristbands have been used with some success. Acupressure is a form of massage in which the practitioner uses energy channels, called meridians, to increase energy flow and affect emotions.
    d. Behavioral interventions--such as self-hypnosis, progressive muscle relaxation, biofeedback, guided imagery, cognitive distraction, and systemic desensitization--have been used either alone or in combination with pharmacologic agents to prevent or control chemotherapy-induced nausea and vomiting. These behavioral methods are similar in that their use is an attempt to induce relaxation as a learned response. Each method induces relaxation in a different manner.
    e. Dietary interventions
        1. Encourage the patient to eat small, frequent meals.
        2. Medicate the patient prior to meals so that the antiemetic effect is active during and immediately after eating.
        3. Encourage the patient to avoid fatty, spicy, or highly salted foods or foods with strong odors.
        4. Determine and repeat past measures that have been effective in controlling nausea and vomiting.
        5. Encourage the patient to eat cold or room temperature foods because these give off fewer odors than do hot foods.
        6. Suggest that the patient cook meals between chemotherapy regimens, when he or she is not nauseated, and freeze the meals for later use, or suggest that another family member cook meals.
        7. Avoid favorite foods on the day of chemotherapy and while nausea and vomiting persist so that aversions to the foods do not develop.
        8. Suggest that the patient try foods containing ginger when feeling nauseated. In folk medicine, ginger is known as an agent that decreases nausea and vomiting.
4. Patient and family education
    a. Instruct the adult patient to notify the staff if nausea and vomiting persist for more than 24 hr. or if he or she is unable to maintain fluid intake. Make sure that a pediatric patient´s family knows to notify staff after a few hours of vomiting. In children, just a few hours of vomiting can cause dehydration.

b. Remind patients as necessary to take antiemetics before arriving for treatment. Some patients need more reminders than others.
c. Follow-up 24-48 hr. after outpatient treatment is essential to ensure adherence to or effectiveness of the antiemetic regimen.

B. Diarrhea

1. Assessment: Accurate assessment is crucial in determining the cause and type of diarrhea; knowing cause and type can be crucial to proper treatment (e.g., mistakenly using an antidiarrheal to treat diarrhea caused by infection can intensify diarrhea severity). Likewise, irinotecan causes two distinct forms of diarrhea (early onset cholinergic and late onset), and each requires a different management strategy.
    a. Assess stools
        1. Assess the pattern of elimination and stool character in relation to treatments (i.e., onset, duration, frequency, consistency, amount, odor, color). Chemotherapy-induced diarrhea usually consists of frequent, watery to semisolid stools with an onset 24-96 hr. after chemotherapy administration.
        2. Grade the diarrhea according to National Cancer Institute (NCI) criteria. (NCI Common Toxicity Criteria are cited in Appendix 1 in the original guideline document.)
        3. Watch for the presence of blood or mucus in the stools.
        4. Monitor the patient for incontinence.
    b. Conduct a physical examination: The presence of fever, blood in the stool, abdominal pain, weakness, or dizziness warrant medical attention to rule out infection, bowel obstruction, or dehydration. The steps of a physical examination follow.
        1. Auscultate bowel sounds.
        2. Palpate and assess the abdomen.
        3. Assess the patient for fecal impaction.
        4. Look for signs of malnutrition, dehydration, electrolyte imbalance, and infectious process.
        5. Ask the patient about his or her experience of pain.
        6. Assess the patient for fever, weakness, and dizziness.
        7. Determine if blood has been present in the stool.
    c. Take a diet history.
        1. Find out if the patient´s dietary habits have changed. Be especially aware of clues that indicate that the amount of fiber in the diet has increased rapidly.
        2. Assess patient for intake that could contribute to diarrhea (e.g., irritating foods, alcohol, coffee, fiber, fruit, sorbitol-based gum).
        3. Assess the patient for food or lactose intolerances or allergies.
    d. Take a medication history: Assess the patient for use of the following.
        1. Antacids (especially magnesium-containing compounds)
        2. Antibiotics
        3. Antihypertensives
        4. Potassium supplements

5. Diuretics
6. Caffeine
7. Theophylline
8. NSAIDs
9. Antiarrhythmic drugs
10. Overuse of laxatives or stool softeners
11. Opium or withdrawal from opium
12. Promotility agents (metoclopramide)
13. Magnesium oxide

e. Assess other factors: Ask the patient about:
    1. Travel history (such as to other countries)
    2. Use of alternative therapies, (e.g., dietary supplements, herbal remedies, coffee enemas)

f. Take objective measurements.
    1. Monitor intake and output.
    2. Monitor weight.
    3. Monitor laboratory data.
        - Check stool-culture results to determine if infection plays a role.
        - Check serum chemistries to determine if electrolyte imbalance, specifically the level of potassium, and protein-calorie malnutrition (hypoalbuminemia) play roles.
        - Assess complete blood count (CBC) to determine if infection is present.
    4. Check skin turgor.
    5. Check vital signs.

2. Collaborative management
    a. Monitor number, amount, and consistency of bowel movements.
    b. Replace fluid and electrolytes, including potassium.
    c. Administer antidiarrheal medication as appropriate to reduce stool frequency, volume, and peristalsis. Reassess the severity of chemotherapy-induced diarrhea 8-12 hr. after antidiarrheal medication. Antidiarrheal medications include:
        1. Loperamide: Produces fewer CNS side effects than does diphenoxylate because loperamide does not contain atropine. Loperamide reduces peristalsis in the small and large intestines.
        2. Diphenoxylate: Contains atropine sulfate. Recommended for early-onset cholinergic diarrhea. Should not be used by patients with advanced liver disease.
        3. Octreotide: A synthetic hormone analog used to treat chemotherapy-induced diarrhea when patients do not respond to oral antidiarrheal agents 24-48 hr. after chemotherapy administration. Requires subcutaneous or IV administration and is costly.
3. Patient and family education: Teach the patient and family to:
    a. Know when to start antidiarrheal medications (e.g., with certain chemotherapeutic agents, antidiarrheal medication should be given prophylactically).

b. Eat foods containing pectin, such as bananas, avocados, and asparagus tips (all three are also high in potassium); beets; unspiced applesauce; and peeled apples.
c. Drink ginger tea, which has a high pectin level.
d. Eliminate from the diet foods that are stimulating or irritating to the GI tract (e.g., whole-grain products, nuts, seeds, popcorn, pickles, relishes, rich pastries, raw vegetables).
e. Eat a low-residue, low-roughage, low-fat diet that includes potassium-rich foods. The BRAT diet is such a diet. BRAT stands for bananas, rice, apples (peeled), and toast (dry).
f. Avoid alcohol, caffeine-containing products, and tobacco.
g. Avoid greasy foods, spicy foods (curry, chili powder, garlic) and fried foods.
h. Maintain fluid intake by drinking 8 to 10 large glasses each day of clear fluids (e.g., bouillon; weak, tepid tea; gelatin; and sports drinks). Water alone lacks the needed electrolytes and vitamins. Carbonated caffeine drinks contain relatively few electrolytes and so may worsen diarrhea. Fluids with glucose are useful because glucose absorption drives sodium and water back into the body. Increase the fluid intake of the pediatric patient.
i. Avoid prune juice and orange juice.
j. Eat food at room temperature. Hot and cold foods may aggravate diarrhea.
k. Avoid milk and dairy products.
l. Avoid hyperosmotic supplements (Ensure, Sustacal) that contribute to the production of loose, high-volume stools.
m. Clean the rectal area with mild soap and water after each bowel movement, rinse well, and pat dry with a soft towel. Cleaning decreases the risk of infection and skin irritation. Moisture-barrier ointment may provide additional protection.
n. Take warm sitz baths to relieve pain related to perianal inflammation. Corticosteroid creams or sprays may also help to relieve pain related to inflammation.
o. Know when diarrhea can be self-managed and when to seek help.
p. Report excessive thirst, fever, dizziness or lightheadedness, palpitations, rectal spasms, excessive cramping, watery or bloody stools, and continued diarrhea in spite of antidiarrheal treatment. These symptoms can be life-threatening.
q. Continue with an antidiarrheal therapy, even if the medication seems to be ineffective.

C. Mucositis

1. Assessment: Use a standardized assessment tool when performing a physical examination. Such a tool will increase the validity and reliability of documentation. Three common forms are:

   Oral Assessment Guide (OAG): The OAG contains eight categories that reflect oral health and function (see Table 27 in the original guideline document).

Oral Cavity Assessment Form: This tool uses a numeric rating, 1-4, in each of five categories (lips, tongue, oral mucosa, teeth/dentures, saliva). The total score represents the level of dysfunction: mild (6-10), moderate (11-15), or severe (16-20).

NCI Common Toxicity Criteria: The NCI tool consists of a 0-4 grading index that is associated with descriptions of mucosal changes. See Appendix 1 in the original guideline document.

a. Examine the lips, tongue, and oral mucosa for color, moisture, texture, and integrity.
b. Assess the patient for changes in taste, voice, ability to swallow, and comfort during swallowing.
c. Examine the saliva for amount and quality.

2. Collaborative management
    a. Oral care: In addition to helping maintain health, oral care can improve the patient´s feeling of well-being and quality of life. Oral care consists of:
        1. Preventing infections and periodontal disease
        2. Preventing gingival bleeding
        3. Preventing damage to oral structures
        4. Helping the patient to maintain oral intake
        5. Reducing oral complications to allow for completion of the treatment plan
    b. Prevention
        1. Conduct a pretreatment dental evaluation with attention to potentially irritating teeth surfaces, underlying gingivitis, periodontal infection, and ill-fitting dentures. Crucial dental work should be done before chemotherapy begins. Once therapy begins, neutropenia and thrombocytopenia contraindicate corrective dental work. Removing braces may be necessary if the patient is undergoing transplantation or if prolonged periods of neutropenia are anticipated.
        2. Emphasize intake of high-protein foods and lots of fluids (> 1,500 ml/day) to encourage oral mucous membrane regeneration. Calorie and protein requirements for children are age-specific; see Table 28 in the original guideline document.
        3. Have the patient use cryotherapy (ice chewing) during short chemotherapy infusions to help prevent mucositis.
        4. Administer leucovorin after methotrexate to decrease the risk of mucositis.
    c. Interventions
        1. Encourage the use of oral agents to promote cleansing, prevent infection, moisturize the oral cavity, maintain mucosal integrity, and promote healing (see Table 29 in the original guideline document).
        2. Administer systemic pain medications.
        3. Culture mucosal lesions when they appear. Bacterial, fungal, and viral mucosal lesions look the same. Only by knowing the cause of the lesion can you provide

appropriate treatment. Candidial lesions look like whitish plaques on the mucosa and are often treated while cultures are pending.

3. Patient and family education: Stress the goals of keeping the oral cavity clean, moist, and intact to prevent further damage to the mucosa during myelosuppressive therapy. To do this, the patient should:
    a. Perform a daily oral self-exam: Make sure that the patient knows to report signs and symptoms of mucositis.
    b. Comply with an oral hygiene program: When mild to moderate dysfunction is present, the frequency of oral hygiene should be increased to every 2 hr. If the condition progresses to a more severe dysfunction, hourly care may be indicated. The program should include:
        1. Flossing the teeth daily with nontraumatic dental tape (if not contraindicated)
        2. Brushing the teeth with a soft toothbrush or, during neutropenia or thrombocytopenia, a sponge swab
        3. Cleansing the oral cavity after meals, at bedtime, and at other times by vigorously swishing the mouth with an appropriate cleansing agent (see Table 29 in the original guideline document). Oral rinsing should be done to remove excess debris before applying local anesthetic agents.
        4. Avoiding use of oral irrigators, which may force microorganisms into ulcerated and compromised gingival tissue, leading to bacteremia.
        5. Avoiding irritating agents: Such agents include commercial mouthwashes containing phenol, astringents, or alcohol; harsh toothpastes; hot or spicy foods and beverages; alcohol; tobacco; poorly fitting dentures; braces; and lemon-glycerin swabs and solutions.

D. Anorexia

1. Assessment: Nutrition assessment provides an estimate of body composition (e.g., fat, skeletal muscle protein, and visceral protein). This helps to identify patients who are at risk of cancer-induced malnutrition and to estimate the magnitude of nutrition depletion in patients who are already malnourished.
    a. Assess factors related to food.
        1. Take a diet history.
        2. Ask about food preferences, food intolerances, food aversions, and food allergies.
        3. Encourage the patient to use a food diary to record the amount and types of food and beverages he or she consumes. This is usually done over three consecutive 24-hr. periods. Other means of documenting intake include a food frequency questionnaire, direct observation and recording, and evaluation of nutrient intake according to standard nutrition criteria (such as the Recommended Dietary Allowances).

4. Assess education needs regarding diet and nutrition and psychosocial factors (e.g., family support, religious and cultural factors) that affect the patient´s eating.
5. Determine the patient´s ability to obtain, purchase, and prepare food.

b. Perform a physical examination.
1. Monitor the patient´s height and weight. Compare current measurements with pretreatment measurements. An unintentional weight loss of 10% or more of body weight within the previous six months signifies a substantial nutrition deficit.
2. Assess skin, hair, mouth, teeth, and general muscle tone for signs of nutrition deficiencies. (Look for dry, flaky skin; muscle wasting; pale skin or sclera; unhealed wounds; etc.).
3. Take anthropometric measurements, which quantify body compartments and correlate them with values from age- and sex-matched normal populations. Mid-arm muscle circumference provides a measure of muscle mass. Measurements of subscapular and triceps skinfolds represent an index of body fat. These values may vary with the patient´s hydration status.

c. Evaluate laboratory results. Be aware of the fact that biotherapy, which usually involves an increase in interferon-a, IL-1, TNF, and other cytokines--increases the rate of lipolysis, decreases lipoprotein lipase activity, increases fatty-acid synthesis, decreases insulin receptor tyrosine kinase activity, and increases serum triglyceride levels. These effects may be evident in the lab results of a patient with anorexia who is undergoing biotherapy. In regard to biotherapy and chemotherapy patients, monitor the levels of:
1. Serum transferrin: The level of serum transferrin reflects the body´s ability to make serum proteins. A value < 200 mg/dl reflects acute changes in visceral protein.
2. Serum albumin: Measurements of serum albumin are used to estimate visceral protein levels. A value < 3.5 g/dl indicates protein depletion. Albumin levels may be influenced by body stresses (e.g., trauma, infection), changes in hydration status, and alteration in liver and renal function.
3. Serum prealbumin: The level of serum prealbumin is a sensitive indicator of changes in nutrition status. A level < 15 mg/dl indicates protein depletion.
4. Lymphocyte count: A depleted lymphocyte count indicates decreased immunocompetence.
5. Electrolytes, minerals, trace elements, and vitamins: Levels of these components can help confirm or dispute physical observations. Zinc deficiency can cause taste and smell alterations. A deficiency of magnesium, potassium, or calcium can cause muscle twitching. Pallor can indicate an iron deficiency.

2. Collaborative management: The extent of nutritional intervention depends on the cause of weight loss and the overall goals of the

patient and healthcare team. The goal of nutritional support for the patient with cancer is to prevent or reverse the cachexia of malignancy.

a. Consult a dietitian for help in planning the patient´s diet.
b. Administer high-calorie, high-protein dietary supplements if indicated.
c. Administer megestrol acetate if appropriate. Megestrol acetate increases appetite and lean body mass and decreases the breakdown of fat reserves. The recommended dose is 20 ml (800 mg/day).
d. Administer dronabinol if appropriate. Dronabinol has been found to be an effective appetite stimulant for selected patients with advanced cancer.
e. Administer enteral nutrition if the patient cannot meet caloric requirements by oral intake.
f. Administer total parenteral nutrition (TPN) if GI function is altered or absent or if the patient is intolerant of enteral therapy.
g. Alert the patient to community resources (e.g., Meals on Wheels or the Special Supplemental Nutrition Program for Women, Infants, and Children [popularly known as WIC]) to assist with nutrition.

3. Patient and family education: Teach the patient to:
    a. Weigh himself or herself weekly, using the same scale at the same time of day.
    b. Eat small, frequent meals. Using smaller plates may help the patient overcome the impression that he or she is being asked to eat a great deal.
    c. Incorporate high-protein foods into the diet. Marinate meats to enhance or disguise flavor. Use other high-protein foods (e.g., cheese, milk, eggs, beans, nuts, yogurt, puddings, wheat germ) in place of meat.
    d. Avoid filling and gas-forming foods (e.g., broccoli, cabbage, fruits, carbonated beverages).
    e. Drink fluids with meals to rinse away bad tastes. Fruit-flavored drinks tend to be well tolerated; coffee and tea frequently are not.
    f. Avoid large quantities of liquids that may reduce the intake of solid foods
    g. Eat slowly to allow the stomach to empty while eating.
    h. Medicate him- or herself for pain or nausea to minimize discomfort, if indicated.
    i. Minimize odors that can affect taste by drinking fluids cold and with a straw and by choosing cold foods such as cheese, milkshakes, cold cuts, and tuna and egg salad.
    j. Use hard candies and fresh fruit, if possible, to eliminate bad tastes in the mouth and leave a more pleasant taste.
    k. Plan daily food-preparation activities to conserve energy.
    l. Experiment with approaches to eating and food preparation:
        1. Ordering take-out, preparing large quantities and freezing portions for later
        2. Purchasing frozen dinners
        3. Varying the surroundings (e.g., dining out)

4. Using distractions (e.g., radio, TV)
5. Trying new foods and recipes
6. Arriving at the table immediately before meals, to minimize the effect of food odor on appetite

m. Use gravies or sauces on foods to help spread taste through the mouth and add calories.
n. Use tart foods to help overcome metallic tastes.
o. Use plastic eating utensils and glass or plastic cooking containers if a metallic taste is noted while eating.
p. In the absence of a sodium restriction, use salt to decrease the excessive sweetness of sugary foods.
q. Add a small amount of seasoning to food (e.g., oregano, basil, cinnamon, or ginger) to enhance food flavor. Strongly seasoned foods (e.g., Italian, Mexican, curried, or barbequed dishes) may satisfy the patient who has a diminished sense of taste.
r. Brush the teeth or rinse the mouth before and after meals to keep the mouth clean and reduce bad tastes. If mucositis is a problem, the patient should rinse the mouth with a solution of salt, baking soda, and warm water before eating; the rinse will help eliminate bad tastes.
s. Avoid cigarette smoke or smoking, which can affect the sense of smell, which affects the sense of taste
t. Report symptoms associated with anorexia to the healthcare team.
u. Report physical changes (e.g., fatigue, anemia, mouth sores) that decrease appetite and require management.

E. Constipation
1. Assessment
a. Assess patterns of elimination, including the amount and frequency of elimination and the urge to defecate, character of the stool, volume of stool, chronic use of laxatives or softeners, other measures to enhance bowel function.
b. Assess the patient´s usual dietary pattern, focusing on fluid and fiber intake.
c. Assess mobility, activity level, and functional status.
d. Assess abdominal pain or cramping.
e. Determine facts about the patient´s last bowel movement: When, amount, consistency, color, presence of blood.
f. Determine current medication usage.
g. Use laboratory results to assist in metabolic evaluation.
h. Perform abdominal palpation and rectal examination. A rectal examination is not routinely performed if the patient is a child.
i. Use radiographs to differentiate between mechanical obstruction and decreased motility from an ileus.
2. Collaborative management
a. Administer laxatives as ordered. Use laxatives from the following groups:
1. Bulk-forming laxatives: Cause water to be retained in the stool. Of limited use for patients who cannot tolerate at least 3 liters fluid each day.
2. Lubricants and emollients: Coat and soften the stool. Excessive doses can lead to rectal seepage and perianal irritation.

3. Saline laxatives: Contain magnesium or sulfate ions. Act by drawing water into the gut. Of little use in a daily prevention program. Used most often for acute evacuation of the bowel.
4. Osmotic laxatives: Include lactulose and sorbitol. Excessive amounts result in watery diarrhea.
5. Detergent laxatives: Have a direct action on the intestines by allowing water and fats to penetrate into dry stool. Decrease electrolyte and water absorption from the colon. Of little value in a prophylactic bowel management program for long-term constipation. Appropriate for short-term use when straining is to be avoided.
6. Stimulant laxatives: Act directly on the colon to stimulate motility and are activated by bacterial degradation in the intestine. The most commonly used in a prophylactic plan.
7. Suppositories: Stimulate the intestinal nerve plexus and cause rectal emptying. Not indicated for long-term bowel management.

b. Use a combination laxative-stool softener prophylactically for patients receiving vinca alkaloids.
c. Include an increase in physical activity or passive exercise as appropriate in a bowel-retraining regimen. These promote the urge to defecate by helping to move feces into the rectum.
d. Help the patient maintain usual bowel habits during hospitalization. Provide privacy and comfort.
e. Increase fluids and fiber, and begin management with oral medications to help constipated patients with neutropenia or thrombocytopenia.
f. Patients with neutropenia should not have rectal exams or use suppositories or enemas. Doing so could introduce bacteria into the rectum or lead to anal tears, fissures, or abscesses.
g. Do not perform rectal exams or use suppositories or enemas in treating a patient with thrombocytopenia; doing so may increase the risk of bleeding.

3. Patient and family education: Teach the patient to:
   a. Increase fluid intake: Encourage the patient to drink at least eight glasses of fluid daily unless medically contraindicated. Warm liquids before a defecation attempt may be helpful to stimulate bowel movement. Use of coffee, tea, and grapefruit juice is usually discouraged because these beverages act as diuretics.
   b. Increase fiber in diet: Fiber causes feces to pass through intestines more rapidly and decreases the occurrence of fecal impaction. High-fiber foods include bran, popcorn, corn, raisins, dates, vegetables, fruits, and whole grains. Warn patients that they may experience abdominal discomfort, flatulence, or erratic bowel habits in the first few weeks after increasing fiber. Fiber tolerance will develop and such effects can be minimized by slowly titrating fiber consumption, starting with the addition of 3-4 g/day and increasing to 6-10 g/day. This approach is contraindicated in cases of structural bowel blockage, because

increasing bulky intraluminal contents may increase the obstruction.
    c. Encourage the patient to exercise regularly: GI motility is stimulated by regular exercise.
    d. Teach diaphragmatic breathing and abdominal muscle exercises: These help increase muscle tone, which is necessary for defecation.
    e. Help the patient to develop a regular bowel program.
    f. Instruct the patient to report constipation and to be aware of the complications associated with constipation, such as fecal impaction. Stress that the patient should call a physician if three days pass without the patient having a bowel movement.

F. Perirectal cellulitis
  1. Assessment
    a. Ask the patient if he or she is experiencing perineal and/or rectal discomfort. Be alert to fear of defecation, which may signal discomfort the patient is hesitant to mention.
    b. Monitor the patient for the presence of fever.
    c. Perform a physical examination of the perineal area.
      1. The entrance site for the infective agent may be a small tear that shows minimal irritation; you may see gross swelling and inflammation of the perirectal area.
      2. Look for and document tissue sloughing and necrosis.
  2. Collaborative management
    a. Ensure that antibiotic coverage includes a specific antianerobic agent, such as clindamycin or metronidazole, in addition to broad-spectrum aerobic coverage.
    b. Administer antipyretic medications to relieve fever.
    c. Encourage the patient to take sitz baths or use perineal irrigation to help heal the area.
    d. Use 5% lidocaine jelly and/or IV pain medication to control pain.
    e. Administer stool softeners and encourage the patient to eat a low-bulk diet.
    f. Inspect the perirectal mucosa frequently for any signs of irritation or skin breakdown.
  3. Patient and family education
    a. Teach the patient and/or family to:
      1. Maintain meticulous perineal hygiene, especially in the presence of neutropenia
      2. Apply appropriate barrier creams and medicated creams
      3. Monitor him- or herself carefully for any signs of infection or worsening of tissue integrity
    b. Ensure that the patient and family are able to:
      1. Identify the risk factors for perirectal cellulitis
      2. Implement measures that minimize the risk of developing perirectal cellulitis
      3. Identify situations that require prompt professional intervention:
        - Pain, redness, or swelling in the affected area
        - Body temperature $\geq$ 38.6Â°C (101.5Â°F)

Pancreatitis

A. Assessment: In addition to performing a physical examination to find and document the preceding clinical manifestations, ask the patient if he or she is experiencing pain. Pain from pancreatitis may be epigastric or appear in other areas of the abdomen. The pain may radiate to the flank, back, or substernal area. If vomiting is associated with pancreatitis, vomiting does not relieve the pain.
B. Collaborative management
    1. Hold or discontinue any agent that may be the cause of the condition.
    2. Monitor serum lipase and amylase levels.
    3. Ensure that an abdominal ultrasound image of the patient is available.
    4. Provide effective pain control.
    5. Administer antibiotic therapy.
    6. Place an NG tube and implement nothing-by-mouth (NPO) orders to rest the gut during the acute phase of pancreatitis.
    7. Administer fluid and/or electrolyte replacement and/or volume expanders if the patient is in shock.
    8. Ensure bedrest.
    9. Ensure that the patient follows a bland, low-fat diet when food can be reintroduced.
    10. Monitor vital signs, level of consciousness (LOC), and condition carefully for signs of shock or electrolyte imbalance.
C. Patient and family education: Teach the patient to:
    1. Use analgesics correctly, for control of pain
    2. Implement effective oral and nasal care while NPO with an NG tube
    3. Know the importance of adherence to dietary and pharmacologic recommendations
    4. Recognize the early symptoms of pancreatitis and seek medical intervention immediately if the symptoms appear

Alopecia

A. Collaborative management: Alopecia can be so traumatic for a patient that he or she might consider refusing therapy because of it. There is no known preventive or treatment for alopecia caused by cytotoxic therapy.
    1. Scalp hypothermia, although used in the past with mixed results, is no longer recommended. Reducing circulation to the scalp may create a sanctuary site for cancer cells.
    2. Vitamin E is ineffective.
B. Patient and family education: Provide information about:
    1. The cause of alopecia and the time frame of hair loss and regrowth.
    2. Strategies to manage hair loss. These include instruction about gentle hair care and the need to avoid permanent-wave and coloring agents, vigorous brushing, and roller and hair-dryer use. Explain the need to protect the scalp from cold and sun.
    3. Local resources for support (e.g., wig salons, scarf and turban catalogs, support groups). If possible, refer interested patients to Look Good ... Feel Better, a program offered by the American Cancer Society. The program provides guidance about wigs and other head coverings, make-up, etc.

Fatigue

A. Assessment
    1. Assess the impact on activities of daily living (ADL): Distinguish between acute and chronic fatigue.
        a. Acute: Intermittent symptoms that last less than one month.
        b. Chronic: Extreme, generalized weakness or lack of energy that lasts longer than one month.
    2. Assess coexisting medical conditions, including anemia, hypertension, diabetes, thyroid or metabolic disorders, electrolyte imbalances, infection, and menopause.
    3. Assess for use or nonuse of medications that contribute to symptoms, including vitamins, caffeine, alcohol, and recreational drugs.
    4. Assess for benefits and risks if patient is using complementary and/or alternative therapy (e.g., diet modification, herbal therapy, mind-body interventions, bioelectromagnetic therapies).
    5. Assess fatigue level.
        a. In adults:
            1. Solicit the patient´s description of fatigue according to a linear analog scale (0-10, with 0 = not tired, full of energy, and peppy; 10 = total exhaustion).
            2. Determine the onset and duration of fatigue.
            3. Determine the pattern of fatigue (i.e., intermittent versus constant).
            4. Determine enhancing and alleviating factors.
            5. Determine associated factors (e.g., pain, stress).
        b. In children:
            1. Solicit the patient´s description by using yes/no questions and the intensity scale that follows. Fatigue is: 1 = not a problem, 2 = sometimes a problem, 3 = often a problem.
            2. Assess the expectations of the patient´s family in regard to the child´s level of involvement in usual activities.

B. Collaborative management
    1. Evaluate ADL and encourage the patient to balance exercise, rest, and energy-enhancing activities.
    2. Collaborate with the physician to correct the potential causes of fatigue (e.g., dehydration, anemia, electrolyte imbalances, oxygenation).
    3. For the patient and family, provide anticipatory guidance about symptoms. Develop an individualized care plan.
        a. Encourage the patient and family to reorganize activities and work schedules to decrease or eliminate low-priority activities.
        b. Evaluate medications that may contribute to fatigue and develop strategies to offset the effects (e.g., add caffeine with pain medications).
    4. Obtain a nutrition consultation as needed.
    5. Discuss and/or pursue a rehabilitation and/or physical therapy consultation, as needed.
    6. Discuss and/or pursue a consultation with a psychiatric nurse, social worker, psycho-oncologist, or psychiatrist, as needed.
    7. Collaborate with the healthcare team to reduce demands (e.g., interruptions, competing stimuli) on a pediatric patient.
    8. Collaborate with the parents of a pediatric patient to identify causes of the child´s fatigue (e.g., treatment environment, family schedule) and factors that could alleviate it (e.g., planning events when the child is at

peak energy level; providing distractions that are pleasing to the child; or offering food supplements, such as milkshakes or finger foods).

C. Patient and family education
    1. Provide information about the causes and contributing factors of fatigue.
    2. Encourage the patient and significant others to set goals based on realistic abilities and limitations.
    3. Encourage the patient to ask for help with personal responsibilities as needed.
    4. Encourage the patient to keep an activity-fatigue journal to identify patterns of energy and fatigue during the day.
    5. Instruct the patient and family about strategies for dealing with and alleviating fatigue based on baseline functional status.
    6. Encourage the patient to do aerobic exercises regularly if there are no medical contraindications (i.e., lytic bone lesions, thrombocytopenia, cachexia).
    7. Encourage the patient to take short, frequent rest periods.
    8. Encourage the patient to perform energy-enhancing activities (e.g., meditation, yoga, visualization, listening to relaxation tapes, relaxing in a pleasant outdoor place).
    9. Encourage the patient and significant others to prioritize activities and plan high-priority activities at times of increased energy.
    10. Encourage the patient to eat a balanced diet based on the "food pyramid."
    11. Encourage the patient to keep a regular sleep schedule.
    12. Encourage the patient and family to maintain a moderate-temperature environment.
    13. Instruct the patient to report changes in energy level to his or her healthcare provider.

Cardiac toxicity

Table 30 in the original guideline document lists cardiotoxic chemotherapeutic drugs by category.

A. Assessment before biotherapy:
    1. Before treatment with IL-2: Ensure that the patient has undergone a baseline cardiac evaluation of left ventricular function to determine his or her eligibility for treatment with IL-2.
    2. Before treatment with certain monoclonal antibodies (e.g., trastuzumab): Ensure that the patient has undergone a MUGA or ECG to establish baseline cardiac function.

B. Assessment throughout therapy, especially for high-risk patients:
    1. Check the results of baseline cardiac studies (e.g., ejection fraction) before administering the drug.
    2. Observe the patient for clinical manifestations of CHF (e.g., tachycardia, shortness of breath, nonproductive cough, neck-vein distention, ankle edema, gallop rhythm, rales, hepatomegaly, cardiomegaly).
    3. Calculate and assess the cumulative dose of the applicable drug (e.g., doxorubicin), and document it in the patient´s records.

4. Assess heart rate, rhythm, and regularity, including murmurs, split sounds, and extra sounds (a gallop, or third heart sound, may indicate insufficiency).
5. Assess electrolytes (e.g., potassium, calcium); abnormal electrolytes can interfere with cardiac function.

C. Collaborative management

1. Administer, if part of the protocol in your institution, cardiac-protective iron-chelating agents (e.g., dexrazoxane) during or prior to the administration of the chemotherapeutic drug to prevent doxorubicin-induced cardiotoxicity in some patients (e.g., patients with metastatic breast cancer who have received 300 mg/m^2 doxorubicin). Iron-chelating agents inhibit the generation of free radicals. It has been reported that dexrazoxane significantly decreased cardiac toxicity in children when the drug was administered in pediatric trials. Additional trials involving pediatric patients are ongoing. Dexrazoxane has also reduced cardiac toxicity in adults; the FDA has approved it for limited use by adults.
2. Administer medications as prescribed to treat CHF, and support cardiac output (e.g., use diuretics, inotropic cardiac medications, vasodilators, and/or oxygen).
3. Metoprolol tartrate, a beta-blocker, has been used effectively to treat pediatric patients who have severe CHF following doxorubicin therapy.
4. Develop an activity or exercise plan.
5. Institute dietary modifications (e.g., a low-salt diet), as necessary for CHF.
6. Instruct the patient to avoid tobacco and alcohol use because these agents stimulate cardiac muscle.
7. Expect to discontinue or reduce the dose of the antineoplastic agent if the patient´s ejection fraction is less than 55%.
8. Monitor results of ECGs; for a chemotherapy patient, an ECG is recommended at three months, six months, and one year post-anthracycline therapy.
9. Monitor results of MUGA scans; for a chemotherapy patient, a scan is recommended every five years.

D. Patient and family education

1. Teach the patient that cardiotoxicity is a possible side effect of the drug(s) (e.g., anthracyclines [doxorubicin, daunorubicin and liposomal daunorubicin, mitoxantrone]; high-dose fluorouracil; high-dose cyclophosphamide; and interleukins, interferons, and some monoclonal antibodies); see Tables 30 and 21 in the original guideline documents.
2. Instruct the patient about the signs and symptoms of CHF and when to report to a nurse or physician; explain that close monitoring of possible late effects may be required even after treatment has ended.
3. Instruct the patient that chronic cardiac toxicity usually is dose-related and possibly irreversible.
4. Instruct the patient and family about strategies they can use to manage symptoms at home.
5. Ensure that the patient is familiar with the ongoing protocol for follow-up care:
    a. Each year, a standard physical and history
    b. Every two to five years, MUGA scans and/or ECG. The number of risk factors should determine the interval between such tests.

c. Every three years, 24-hr. Holter monitoring
d. Before pregnancy, general anesthesia, or the start of a vigorous exercise program, a cardiology consult.

6. Encourage a healthful lifestyle that eliminates tobacco and alcohol and includes exercising regularly and maintaining an appropriate weight and nutritional diet.
7. Stress the importance of lifelong follow-up care with a healthcare provider familiar with the patient´s cancer history, treatment, and risk of late effects.

Pulmonary toxicity

A. Pretreatment assessment for biotherapy: Pulmonary function testing is a prerequisite for the following patients being evaluated for biotherapy (particularly for treatment with IL-2):
   1. Heavy smokers
   2. Patients with extensive pulmonary disease
   3. Patients with symptoms suggesting decreased pulmonary reserve
B. Assessment: The following assessment steps may not apply if the patient is an inpatient receiving IV IL-2 or vasopressors or is an outpatient receiving subcutaneous IL-2.
   1. Percuss and auscultate the lungs. Assess location and degree of adventitious breath sounds (e.g., rales, rhonchi, wheezes, rubs).
   2. Assess depth, rhythm, and effort of respiratory breathing.
   3. Note chest symmetry and retraction of intercostal muscles.
   4. Note accessory muscle use.
   5. Determine the presence of a cough and the amount, color, and productive nature of sputum.
   6. Note skin and mucous membrane color (dusky, ashen, or cyanotic).
   7. Monitor the results of pulse oximetry and arterial blood-gas tests.
   8. Observe the abdomen for distention. If the abdomen presses on the diaphragm, breathing is more difficult.
   9. Assess the patient for chest and/or back pain and evaluate possible causes. Possible causes include pleural effusion, pulmonary embolism, and pneumothorax, all of which require medical attention.
   10. Assess and document LOC.
   11. Obtain chest radiographs. Frequency depends on patient and therapy.
   12. Monitor pulmonary function tests.
C. Collaborative management: Because lung damage is often irreversible, early detection and prevention of pulmonary toxicity are imperative.
   1. If pulmonary toxicity is suspected, hold chemotherapy and notify a physician.
   2. Do not use fluid boluses if patient is in respiratory distress (e.g., showing signs of dyspnea or increasing crackles).
   3. Initiate fluid restriction if pulmonary edema is problematic; administer IV colloidal therapy as ordered.
   4. Keep strict intake and output records for all patients receiving IV IL-2.
   5. Administer corticosteroids and antibiotics as ordered. Corticosteroids usually are contradindicated for patients receiving biotherapy.
   6. Elevate the head of the patient´s bed if signs of respiratory compromise appear.

7. Provide supportive therapy (e.g., vasopressors, diuretics, and/or artificial ventilation) for acute episodes.
8. Provide oxygen therapy when ordered; however, when using bleomycin, be aware of reports of oxygen-induced lung damage.
9. Monitor the patient´s weight.
10. Monitor the adequacy of diuresis after the patient has finished IL-2 therapy. Heart rate and blood pressure should be within acceptable limits.
11. Follow-up recommendations:
    a. Monitor pulmonary function tests as indicated.
    b. Obtain chest radiographs; a radiograph may be recommended every one to two weeks to monitor for bleomycin.

D. Patient and family education
1. Provide patient and family education regarding symptoms associated with pulmonary toxicity (e.g., cough, dyspnea, chest pain, shallow breathing, chestwall discomfort). Make sure all patients, including outpatients receiving subcutaneous IL-2, know to seek medical assistance immediately if symptoms begin.
2. Ensure that a biotherapy patient knows the effects of cytokines before biotherapy begins.
3. Make sure a biotherapy patient knows that IL-2 may be delayed or held until pulmonary symptoms resolve.
4. Explore with the patient his or her wishes regarding intubation and resuscitation status; establish advance directives.
5. Teach the patient that raising the head of the bed may facilitate breathing.
6. Instruct the patient to conserve energy by performing daily activities when his or her energy level is highest.
7. Teach the patient and family methods to decrease symptoms of dyspnea by exercising to tolerance, practicing pursed-lip breathing, refraining from smoking, and using a small fan.
8. Teach the patient to take an opioid (in most cases, morphine) as prescribed by his or her physician; opioids may relieve the discomfort caused by air hunger.
9. If at risk for pulmonary edema, teach the patient to restrict fluid.
10. Review the safety issues (e.g., flammability) related to oxygen administration.
11. Upon discharge, ensure that the patient knows to notify the physician if dyspnea, cough, or fever develops.

<u>Hemorrhagic cystitis</u>

A. Assessment: Obtain a baseline urinalysis before therapy and monitor subsequent urinalysis results.
B. Collaborative management
1. Preventive measures for hemorrhagic cystitis
    a. Assess baseline blood urea nitrogen (BUN) and creatinine and the results of routine urinalysis and urine cultures as needed to rule out renal pathology and infection.
    b. Instruct adult patients to increase oral fluid intake; provide parenteral hydration if the patient is unable to drink and retain oral fluids. Instruct adolescent patients to increase oral fluid

intake to 3 liters per day. Provide vigorous IV hydration if a patient is unable to drink and retain fluid. Hydration should begin 12-24 hr. prior to chemotherapy. Urinary output should be > 100 cc/hr/m^2. Prevention for pediatric patients also includes forced diuresis and administration of chemoprotectant agents.

c. Encourage frequent voiding, day and night.
d. With high-dose cyclophosphamide and any dose of ifosfamide, administer a bladder-protecting mesna. Mesna binds to drug metabolite, inactivating it and allowing it to be flushed from the bladder.
    1. For adults
        - Mesna dosing as protection against the effects of ifosfamide should be 20%-39% of the ifosfamide dose. Administer mesna 15 min. before and at 4 and 8 hr. after ifosfamide. Alternatively, mesna can be administered with ifosfamide, as a continuous infusion at 100% of the ifosfamide dose, following a loading dose of 20%-39% of the ifosfamide dose.
        - Mesna dosing as protection against the effects of high-dose cyclophosphamide should be 60%-120% of the cyclophosphamide dose. Administer mesna 15 min. before and at 4 and 8 hr. after the cyclophosphamide dose.
    2. For children: An IV mesna dose for a pediatric patient is typically 60% of the ifosfamide or cyclophosphamide dose; some studies recommend a 1:1 ratio. The most common pediatric administration schedule consists of IV mesna 15 min. prior to chemotherapy and at 4 and 8 hr. after chemotherapy.

2. Administer final daily dose of oral cyclophosphamide prior to 4 pm, to allow the drug to pass through the bladder prior to bedtime.

C. Management of hemorrhagic cystitis

1. Discontinue ifosfamide or cyclophosphamide administration if evidence of gross hematuria or cystitis is noted.
2. Catheterize the patient.
    a. If the patient is an adult, place a three-way Foley catheter to provide continuous irrigation with saline or acetylcysteine.
    b. In circumstances where clots obstruct the patient´s ability to void, place a large-bore urethral catheter to provide irrigation with a saline solution.
3. Administer aminocaproic acid. The goal is to promote clotting.
4. Obtain a urology consultation. Electrocautery or cryosurgery may be used to control bleeding; cystectomy may be necessary for last-resort cases.
5. Follow-up recommendations:
    a. Periodic and at least annual urinalysis, urine cytology, and cystoscopy
    b. Periodic excretory urograms for patients with gross hematuria, new microhematuria, abnormal cytologic findings regarding the urine, or persistent irritative voiding

D. Patient and family education

1. Tell the patient about the possibility of hemorrhagic cystitis with ifosfamide and cyclophosphamide regimens.
2. Ensure that the patient knows the signs and symptoms to report.
3. Encourage the patient to void at least every 2 hr. and to take oral cyclophosphamide early in the day, with the last dose before 4 pm.
4. Instruct the adult patient to drink six to eight glasses of fluid each day. Encourage the pediatric patient to increase fluid intake.

Hepatotoxicity

A. Assessment
    1. Obtain a history regarding alcohol intake, documenting specific quantity used.
    2. Determine if the patient is using hepatotoxic over-the-counter or prescription medication.
    3. Obtain a baseline liver function test before beginning therapy. Assess subsequent liver function tests and monitor consecutive levels.
B. Collaborative management
    1. Chemotherapy may be reduced based on elevated liver function studies. However, reducing chemotherapy is controversial because of the paucity of studies validating the practice. Reduction may be valid in cases of chemotherapy:
        a. Involving doxorubicin and, in children weighing up to 12 kg, dactinomycin
        b. For patients with multiple liver-function test abnormalities or direct bilirubin elevation > 2.0 mg/dl
        c. For obese patients (patients whose body weight is 130% or more of ideal body weight). Obese patients eliminate doxorubicin more slowly than do patients of normal weight. Therefore, the drug exposure of an obese patient can be up to twice that of a nonobese patient receiving the same dose.
    2. Avoid using hepatotoxic drugs other than chemotherapeutic agents if liver-function test results are abnormal.
    3. Assess the patient for signs of bleeding.
    4. Assess the patient´s LOC, checking for signs of liver failure or hepatic coma.
    5. Schedule the patient for a full blood chemistry screening that provides CBC, bilirubin and transaminase levels, and clotting time.
    6. Consider the usefulness of a liver biopsy.
    7. Help the patient follow a low-fat, high-glucose diet containing vitamin B and C additives. If the patient is experiencing nausea and vomiting, implement an NPO protocol and administer antiemetics and IV hydration.
    8. Encourage bedrest.
    9. Administer corticosteroids as ordered.
C. Patient and family education
    1. Inform the patient and family that hepatotoxicity is a possible side effect of selected chemotherapy agents.
    2. Tell the patient to avoid alcoholic beverages if hepatotoxicity is noted.
    3. Instruct the patient about the signs and symptoms of liver failure (e.g., jaundice, liver tenderness, changes in urine or stool color).
    4. Promote rest.

5. Encourage the patient to use soothing lotions and cool baths to promote skin comfort. Remind the patient not to scratch.
6. Suggest the wearing of lightweight, loose clothing.
7. Encourage the patient to continue eating a light, high glucose diet.
8. Reinforce the importance of the patient having lifelong annual follow-up assessments performed by a healthcare provider familiar with the survivor´s cancer history, treatment, and risk of developing late effects.
9. Encourage the patient to have liver function tests periodically. Encourage the patient to schedule a physical exam, abdominal ultrasound test, or abdominal computed tomography (CT) scan to establish the etiology of chronic abnormalities revealed by liver function tests.

Nephrotoxicity

A. Laboratory values: For pediatric patients, reference ranges are age-specific. Reference ranges differ from institution to institution. Similarly, indications to hold or delay chemotherapy for pediatric patients are based on evidence of nephrotoxicity as defined by treatment protocol. Consult institution guidelines in regard to specific pediatric cases. The values cited in this section apply to adults only.
    1. BUN
        a. Assess baseline and consecutive levels.
            1. For patients not requiring vasopressors, monitor levels daily.
            2. For inpatients requiring vasopressors, monitor levels twice daily.
            3. For outpatients, monitor levels weekly or as clinically indicated.
        b. Make a rough estimate of renal function. (BUN is very sensitive to hydration status and increases with the level of dehydration.)
        c. Chemotherapy is usually held if serum BUN is > 22 mg/dl.
    2. Serum creatinine
        a. Assess baseline and consecutive levels. If the patient is on a research protocol, refer to research guidelines.
            1. For patients not requiring vasopressors, monitor levels daily.
            2. For inpatients requiring vasopressors, monitor levels twice daily.
            3. For outpatients, monitor levels weekly or as clinically indicated.
        b. Serum creatinine is a specific and sensitive indicator of renal function.
        c. Chemotherapy is usually held if serum creatinine is > 2 mg/dl.
    3. 12-hr. creatinine clearance
        a. Assess baseline and consecutive levels. If the patient is on a research protocol, refer to research guidelines.
        b. The 12-hr. creatinine clearance can be the most sensitive test of renal function. The 12-hr. test is as effective as the 24-hr.

test and less costly. For pediatric patients, a test of nuclear glomerular filtration rate (GFR) is frequently used.
        c. Accuracy depends on collecting all urine in a specified time.
        d. Chemotherapy usually is held if creatinine clearance is < 60 ml/min. or as indicated by the chemotherapy protocol or guidelines.
    4. Urine cytology: Urine cytology is inaccurate if patients are cachectic.
        a. Assess changes in urine cytology (e.g., RBCs, WBCs, epithelial cells).
        b. Assess for tubular damage.
    5. Urine protein: Proteinuria indicates damage to the glomerular and tubular systems.
    6. Urine-specific gravity and osmolality
        a. A measure of renal ability to concentrate or dilute urine
        b. Indicates presence or absence of tubular and/or medullary damage
    7. Urine pH
        a. A measure of the free hydrogen-ion concentration in urine
        b. Expresses the strength of the urine as a dilute acid of a base solution
    8. Hematuria
    9. Serum electrolytes, especially magnesium, uric acid, and potassium levels
        a. Measure serum electrolytes when giving high-dose chemotherapy, especially cisplatin, and if the patient is at risk for tumor lysis syndrome (TLS).
        b. Monitor serum electrolytes during biotherapy, at the following frequencies:
            1. For patients not requiring vasopressors, monitor levels daily.
            2. For outpatients, monitor levels weekly or as clinically indicated.
        c. Assess patient for fluid imbalance.

B. Objective physical assessment data
    1. Monitor intake and output.
    2. Monitor weight changes, especially weight gain and edema, daily or as clinically indicated.
    3. Monitor the patient for changes in LOC, mental status, or behavior.

C. Collaborative management
    1. General strategies
        a. Monitor renal function tests regularly.
        b. Institute hydration of approximately 3 liters/day to prevent or minimize renal damage, especially with cisplatin and high-dose methotrexate regimens. Hydration for pediatric patients is 1.5 to 2 times maintenance.
        c. Stop or delay drug if BUN or creatinine do not return to baseline.
        d. Treat oliguria judiciously with fluid boluses.
        e. Replace electrolytes as indicated.
    2. Follow-up recommendations
        a. Conduct periodic evaluation, including urinalysis, creatinine clearance, and serum chemistries.

b. Refer patient to a nephrologist, if damage is severe, to assess damage and possibly provide further workup and treatment (e.g., hemodialysis).

3. Drug-specific prevention strategies
   a. Cisplatin regimens
      1. Induce diuresis with either mannitol or furosemide before or after administering cisplatin.
      2. Consider amifostine for reduction of nephrotoxicity associated with cisplatin-based regimens. Amifostine is a naturally occurring thiol that can protect cells from damage by scavenging free radicals and donating hydrogen to repair damaged target molecules. It is rapidly metabolized, with a half-life of 8 min. The usual dose is 910 mg/m^2 IV over not more than 10-15 min., given 30 min. prior to cisplatin. Toxicities include hypotension, nausea and/or vomiting, flushing, and fever/chills; manage by pretreating with antiemetics, adequate hydration, and reclining the patient during and immediately after infusion. Oral and subcutaneous routes are currently under investigation.
   b. High-dose methotrexate (> 100 mg/m^2) regimens
      1. Maintain alkalinization of urine by adding sodium bicarbonate to IV fluids. Assess urine pH after each void, or every 6 hr. if patient is catheterized. Various authors cite various target pHs but agree that urine pH should be, at minimum, $\geq$ 6.5 to 8.0.
      2. Administer leucovorin rescue within the recommended time frame.
      3. Avoid vitamin C, aspirin, NSAIDs, penicillins, and sulfa drugs 48 hr. before and after methotrexate.
      4. Discontinue treatment with trimethoprim and sulfamethoxazole until the methotrexate level has decreased.
      5. Reduce subsequent doses based on degree of toxicity.
   c. IL-2 and interferon administered on an outpatient basis: Encourage the patient to drink 2-3 liters noncaffeinated fluid daily.
   d. IL-2 on an inpatient or outpatient basis: Hold or discontinue IL-2 therapy if:
      1. Urine output is < 10-20 cc/hr.
      2. Renal impairment is persistent
   e. Other regimens
      1. Be vigilant concerning renal toxicity in patients with a large tumor burden and specific diseases and treatments (e.g., acute and chronic leukemias, high-grade lymphoma, small-cell lung cancer, bone marrow transplantation [BMT], and tumor lysis syndrome [TLS]).
      2. Administer allopurinol to decrease uric acid production, which can rapidly lead to acute uric acid nephropathy and renal failure if untreated; discontinue allopurinol when WBC count < 1,000/mm^3.
      3. Administer renal-dose dopamine at 2 mcg/ kg/min. to patients receiving IV IL-2.

D. Patient and family education
    1. Ensure that the patient understands the reasons for changes in urine output, electrolyte depletion, and increasing creatinine and BUN.
    2. Tell the patient that nephrotoxicity is a risk associated with certain cytotoxic agents. Reassure the patient by saying that impaired renal function is usually temporary and reversible.
    3. Reinforce the importance of complying with preventive measures.
    4. Reinforce the importance of collecting 12- and 24-hr. urine for creatinine clearance. If nuclear GFR is used, explain the technique and rationale pertaining to the procedure.
    5. Encourage the patient to increase fluid intake; intake should be 2-3 liters noncaffeinated fluid daily.
    6. Ensure that the patient understands the need to comply with instructions to alkalinize urine and complete leucovorin rescue, allopurinol therapy, and/ or amifostine treatment.
    7. Ensure that the patient understands the reason for weight gain during therapy and the need for diuresis after therapy is completed.
    8. Instruct the patient to avoid the use of drugs that potentiate renal dysfunction.
    9. Give the patient a copy of Eating Hints for Cancer Patients, which is available online from the National Cancer Institute at www.cancer.gov.
    10. Ensure that outpatients receiving subcutaneous IL-2 or interferon know to notify the healthcare team if:
        a. They are unable to make urine for more than 12 hr.
        b. Urine becomes very dark or concentrated
        c. They produce only very small amounts of urine

Neurotoxicity

A. Assessment
    1. Assess behavioral and cognitive functioning.
    2. Determine if behavioral or cognitive changes may be due to the side effects of medications.
    3. Assess patient and family coping.
    4. Assess the patient´s environment to ensure safety at the impaired level of function.
B. Collaborative management: See Table 35 in the original guideline document.
    1. Before biotherapy, perform a baseline neurologic assessment.
    2. Use assessment guidelines for early detection and treatment. Reduce drug dose or discontinue drug as ordered when neurologic deficits are noted (e.g., fine motor losses, numbness, tingling, gait disturbances, constipation, change in mentation).
    3. Follow-up recommendations: Be aware that neurotoxicities associated with biologic response modifiers (BRMs) may progress for a few days after discontinuation of therapy. These usually resolve two to three days after completion of therapy but can persist for two to four weeks.
        a. Assess objective and subjective toxicities and subsequent functional impairment.
        b. Provide supplemental nutrition, if needed.
        c. If impairment persists, consider consultation with the appropriate specialist (e.g., neurologist; pain-management

specialist; physical, occupational, or speech therapist; audiologist).

C. Patient and family education
    1. Tell the patient and/or family that neurotoxicity is a possible side effect of selected cytotoxic agents.
    2. Emphasize patient safety as a priority in managing neurotoxicities.
    3. Instruct the patient and/or family about the signs and symptoms of neurotoxicity. Stress the importance of notifying the physician and/or nurse if they occur.
    4. Provide information about the potential side effects of medications that could cause or change neurologic symptoms.
    5. Educate the patient and/or family in regard to any needed referrals, support organizations, adaptations, and rehabilitative strategies.
    6. Ensure that the patient knows the importance of avoiding alcohol and medications that may alter neurologic status.
    7. Teach parents how to refer their child for school re-entry and intervention.

Alterations in sexuality and reproductive function

A. Management of chemotherapy-induced menopause: Ensure that the patient is referred to an endocrinologist if necessary. Thyroid dysfunction and chronic illness can affect reproductive function.
    1. Hormonal agents: HRT--that is, treatment with estrogen--is the most effective intervention for managing symptoms associated with estrogen deficiency. HRT is usually contraindicated for women who have had breast or endometrial cancers, although this matter has become a prominent clinical-practice issue. Clinical trials are needed to determine under what specific conditions HRT is contraindicated.
        a. Estrogen vaginal cream is effective for vaginal dryness and may eliminate dyspareunia. Some systemic absorption may result (it is estimated to be approximately 25% that of a comparable oral dose).
        b. Medroxyprogesterone and low-dose (20 mg) megestrol acetate have been successful in relieving hot flashes. Side effects may affect acceptability and compliance.
    2. Nonhormonal agents: The agents that follow may relieve menopausal symptoms in some patients.
        a. Water-soluble topical agents are available to improve vaginal lubrication. Patients report that newer topical agents, such as Replens and Astroglide lubricants, are superior to K-Y jelly. Replens appears to increase vaginal moisture and elasticity and returns vaginal pH to the premenopausal state.
        b. Low-dose clonidine (0.1 mg/day), administered either in pill form or by transdermal patch, reduces the frequency and severity of vasomotor symptoms. Dose escalation may improve symptom control but may result in dizziness, nausea, dry mouth, and headache.
        c. Vitamin E is sometimes used by women for the treatment of menopausal symptoms, although studies have not shown a consistent benefit. Recommended dose is 200-800 mg/day.

d. Vitamin B_6 has been reported to have some clinical benefit in the treatment of menopausal symptoms, although no research is available to support its use at this time. Recommended dose is 200-250 mg daily.
e. Bellergal-S tablets--composed of ergotamine, belladonna alkaloids, and phenobarbital--are autonomic stabilizers that reportedly improve menopausal symptoms. Patients should start with one tablet by mouth orally each night and increase the dosage to one tablet twice daily as needed. Side effects may include dry mouth, dizziness, and drowsiness. This medication is potentially addictive.
f. Some reports suggest that the newer antidepressants (e.g., venlafaxine, paroxetine) reduce hot flash severity, but further evaluation of this claim is needed.
g. Herbal therapies are commonly used by women to reduce menopausal symptoms. Some popular herbs include evening primrose, black cohosh, angelica (dong quai), ginseng, and licorice root. Encourage a woman to discuss these remedies with her physician.
h. Diet modifications, including increased soy and flax intake, may ameliorate menopausal symptoms. These foods contain phytoestrogens that affect estrogen levels. The impact of soy and flax on women with breast and endometrial cancer is unknown.
i. Relaxation techniques; exercise; cold compresses to the neck; layering of clothing; avoiding alcohol, caffeine, and spicy foods; and reducing intake of refined sugar may improve symptomatic control of hot flashes.

B. Interventions for adult and older pediatric males
1. Monitor serum follicle-stimulating hormone (FSH) and testosterone levels. This is especially important for men who were treated for Hodgkin´s disease in childhood or early adolescence. Reports indicate that the testosterone levels and bone mineral density of these men decreases over time. Therefore, for them, ongoing evaluation of Leydig-cell function is necessary.
2. Obtain semen analysis to evaluate fertility.
3. Use testosterone replacement if indicated. Two groups of authors reported the success of testosterone replacement. Positive effects include maintenance of bone and muscle mass in older patients. Testosterone treatment may be used to prompt secondary sex characteristics, promote growth and normal body composition and bone density, and enhance the well-being of pubertal patients.
4. Ensure that the patient is referred to an endocrinologist if necessary. Thyroid dysfunction and chronic illness can affect reproductive function.

C. Nursing management of sexual alterations: The PLISSIT Model consists of four stages of intervention and is frequently used for sexual counseling. The four stages are:
1. Permission (P): Ask patients about their sexual or reproductive concerns. This "normalizes" patients´ concerns and opens the door for further dialog.
2. Limited information (LI): Provide specific factual information to clarify concerns and misconceptions and dispel myths.

3. Specific suggestions (SS): Provide specific suggestions based on the patients´ concerns. These may include strategies for improving symptom control and enhancing sexual expression.
4. Intensive therapy (IT): If the three earlier steps are insufficient to manage the patients´ concerns, consider referral to a qualified sex therapist.

D. Patient and family education
1. Provide patients with information regarding contraception, to prevent pregnancy during chemotherapy treatment. Oral contraceptives, used by an older girl or female adolescent, will suppress ovarian function, making the ovaries more resistant to the effects of chemotherapeutic agents and conserving oocytes. Discuss at what time after treatment pregnancy might be appropriate.
2. Explore fertility options prior to initiation of cancer treatment. The nurse may have a role as listener, advocate, educator, and provider of support as a patient considers options.
    a. Nonexperimental options for female patients: Several nonexperimental options exist for female patients facing possible infertility as a result of chemotherapy: in vitro fertilization; gamete intrafallopian transfer; use of donor oocytes, a surrogate gestational carrier, or a surrogate mother; cryopreservation and embryo donation; adoption; and child-free living. Embryo banking is also an option, although it is expensive and not always successful. Points to stress in discussing embryo banking include the following:
        1. The woman must be in the correct phase of the menstrual cycle for eggs to be harvested. The procedure requires hormonal stimulation, which may be contraindicated for women with reproductive malignancies or hormone-dependent tumors.
        2. After harvesting, eggs must be fertilized within 24 hr. Fertilized eggs withstand the thawing and freezing process better than unfertilized eggs and have a higher success rate for producing a pregnancy.
        3. The conception rate associated with embryo banking is approximately 50%.
        4. The legal issues involved, including informed consent.
    b. Experimental options for female patients: Experimental options, such as ovarian tissue harvesting and cryopreservation with subsequent engraftment near the fallopian tube, do exist but are costly. Their success rates are undetermined at this time. Typically, these experimental procedures are not covered by insurance; therefore, they pose an out-of-pocket expense to the patient. When appropriate, discuss the possibility of ova conservation with pubertal girls and their parents.
    c. Nonexperimental option for male patients: Semen cryopreservation provides men an opportunity to father a child even when their sperm count is less than adequate. Even boys who have just achieved puberty may produce sperm that can be cryopreserved for the purpose of reproduction. When appropriate, discuss sperm banking with boys and their parents. Points to include in patient and family education about cryopreservation are:

1. Three to eight specimens collected at 24-hr. intervals should provide an adequate sperm count. Separate harvesting and storage fees generally apply to each collection.
2. The desire to collect sperm for cryopreservation should not significantly delay the patient´s treatment.
3. Discussion of the legal issues, including informed consent, involved in sperm banking.

3. Provide adolescent patients with information about peer support groups that may be helpful in dealing with issues of sexuality and body image.
4. Reinforce the importance of having an annual follow-up examination conducted by a healthcare provider familiar with the patient´s cancer history, treatment, and risk of developing late effects

Cutaneous Reactions

Table 38. Cutaneous reactions

A. Acral erythema
- A painful, erythematous, and edematous rash on the palmar surfaces of the hands and plantar surfaces of the feet.
- General progression to bulla formation, desquamation, and re-epithelialization.
    1. Nursing Assessment
        - Assess potential for acral erythema from risk factors.
        - Inspect palmar and plantar surfaces frequently for sensation, color, movement.
        - Monitor patient for signs and symptoms of infection related to condition.
        - Assess patient for pain and discomfort.
    2. Collaborative Management
        - Apply cold compresses to affected areas to relieve pain.
        - Elevate the affected areas to reduce edema.
        - Apply steroid creams.
        - Administer pyridoxine 50 mg 3 times daily.

B. Hyperpigmentation
- Increased amounts of epidermal melanin without dermal deposition in the skin, hair, nails, mucous membranes, and teeth
    1. Nursing Assessment
        - Assess skin.
        - Assess individual risk factors.
    2. Collaborative Management
        - Encourage patient to use sunscreens for photoprotection.
        - Avoid vasodilation during chemotherapy administration (avoid heating pads, warm compresses).
        - Treat inflammatory skin changes (e.g., dermatitis) promptly to avoid postinflammatory hyperpigmentation.

C. Inflammation of keratoses
- Inflammation of actinic keratoses.

- Pruritus and erythema may be noted adjacent to previous actinic keratoses.
    1. Nursing Assessment
        - Perform a skin assessment of potentially affected areas of actinic keratoses (face, arms, hands, and upper chest).
    2. Collaborative Management
        - Report skin changes to the physician.
        - Distinguish inflammatory reaction from an allergic drug reaction.
        - Monitor patient for local and systemic signs of infection.

D. Nail changes

- May include hyperpigmentation, discoloration, transverse banding, nail grooving (Beau´s lines), and onycholysis (partial separation of nail plate from bed)
    1. Nursing Assessment
        - Assess nails prior to chemotherapy, and note any changes following administration.
        - Assess individual risk factors.
    2. Collaborative Management
        - Instruct patient about potential nail changes, which occur 5-10 weeks after chemotherapy starts.
        - Inform patient that changes are usually temporary (Tenenbaum, 1989). With taxotere, nails eventually fall off.

E. Neutrophilic eccrine hydradenitis

- Tender, erythematous macules, papules, and plaques on the trunk, neck, and extremities.
- May consist of hyperpigmented papules.
- May be associated with a fever with documented infection.
    1. Nursing Assessment
        - Perform skin assessment with specific attention to the trunk, neck, and extremities.
        - Assess for elevated temperature.
    2. Collaborative Management
        - Assess patient for other potential sources of infection when fever is present.
        - Inform the patient that the lesions and associated fever will resolve spontaneously.

F. Radiation enhancement

- A synergistic effect of concurrent radiation therapy and chemotherapy, which augments the effects of the radiation.
- May involve cutaneous edema, erythema, blisters, erosions, ulceration, or hyperpigmentation in radiated field.
    1. Nursing Assessment
        - Perform skin assessment before radiation is initiated and daily thereafter.
        - Assess for individual risk factors.
        - Assess affected area for signs of local infection.
    2. Collaborative Management
        - Instruct patient to avoid trauma and irritation to the affected area.
        - Apply cool, wet compresses if reaction is acute.

- Apply topical steroids as ordered.
- Debride ulcerated areas and apply an antimicrobial ointment and nonadherent dressing over the area.

G. Radiation recall
- An inflammatory reaction occurring in previously irradiated tissue.
- May occur in the skin, lung, gastrointestinal tract, and heart.
    1. Nursing Assessment
        - Perform skin assessment before radiation is initiated and daily thereafter.
        - Assess for individual risk factors.
        - Assess affected area.
    2. Collaborative Management
        - Instruct patient to avoid trauma and irritation to the affected area.
        - Apply cool, wet compresses if reaction is acute.
        - Apply topical steroids as ordered.
        - Debride ulcerated areas and apply an antimicrobial ointment and nonadherent dressing over the area.

H. Hand-and-foot syndrome
- Acral erythema, palmar-plantar erythrodysesthesia syndrome
    1. Nursing Assessment
        - No recommendations presented
    2. Collaborative Management
        - Provide pain control.
        - Apply an ointment (e.g., Bag Balm ointment)

<u>Ocular Toxicities</u>

A. Assessment: Ask the patient about any history of eye disturbance. In addition, assess the following:
    1. Eyelid: Observe and palpate for signs of erythema and edema. Assess for signs of exudates, crusting, and presence of ptosis. Observe condition of lashes.
    2. Conjunctiva: Invert eyelids and observe for hyperemia (engorgement of tissue by blood due to blockage), edema, and discharge.
    3. Cornea: Observe for smooth appearance and clarity. Test corneal reflex by gently touching a cotton swab to corneal surface.
    4. Iris and pupil: Observe iris and pupil. Margins should be clearly identified. Note pain and photophobia.
    5. Lacrimation: Note dryness, foreign-body sensation, and excessive tearing.
    6. Visual disturbances: Assess acuity using near-vision card held at arm´s length; if the patient uses glasses, he or she should be wearing them. Note visual changes, unilateral or bilateral involvement, and precipitating and relieving factors.
    7. Cranial nerves: Observe ocular alignment, light reflex, and extraocular muscles by having the patient follow finger movements in six planes.

B. Collaborative management
    1. Refer the patient to an ophthalmologist or orbital oncology ophthalmologist if signs of toxicity are noted. Routine monitoring for tamoxifen may be indicated if the patient is receiving a higher than

standard dose. A small number of patients have reported changes in visual acuity or the presence of floaters.
2. Recommend eyedrops and lubricants (e.g., dexamethasone eyedrops 0.1%, one drop in each eye twice daily for cytarabine-related conjunctivitis). Cyclosporine eyedrops are now available by prescription.

C. Patient and family education
1. Teach the patient self-examination techniques; emphasize the importance of close monitoring and prompt reporting of any structural changes in eyelids or eyelashes, as well as changes in vision.
2. Emphasize the importance of careful hygiene and handwashing techniques to minimize cross-contamination.
3. Demonstrate the proper use of eyedrops and lubricants.
4. Encourage the patient to have yearly eye examinations. Bone marrow transplantation (BMT) patients and patients with dry eye syndrome may need to be examined as frequently as every six weeks.

Secondary Malignancies

A. Collaborative management
1. Leukemia
    a. Assessment should include looking for signs and symptoms of anemia, bleeding, or frequent infections.
    b. Review CBC, looking for anemia, abnormal WBC count, or thrombocytopenia. If results are abnormal, consider bone marrow aspiration and biopsy with cytogenetics.
2. Breast cancer: Begin mammography screenings and professional breast exams at least 10 years after mantle radiation therapy.
3. Endometrial cancer
    a. Patient should have a gynecologic exam annually.
    b. Any abnormal vaginal bleeding should be investigated by means of an endometrial biopsy.
4. Solid tumors: Assess for palpable mass, pain, bloody stools, anemia, fatigue, and anorexia.
5. CNS tumors: Assess for altered mental state, seizures, headaches, changes in vision, nausea, and vomiting.

B. Education
1. Patient and family education: Tell the patient about the risks of secondary malignancies, the typical time to onset, signs and symptoms of secondary cancers, and the importance of follow-up visits. Ensure that the patient knows to begin having annual mammography screenings and professional breast exams 10 years after mantle radiation therapy.
2. Professional education: Educate primary care professionals who may be working with the patient after the oncologist has stopped following him or her. Ensure that healthcare providers have the same information about secondary malignancies as the patient does and that they are aware of recommended follow-ups.

Post-treatment care

Table 41 in the original guideline document lists the late effects associated with cancer therapy.

A. Nursing assessment
    1. Take a history. Include information about:
        a. Chemotherapy, surgery, and radiation received
        b. Toxicities noted during therapy
        c. Physical and psychosocial systems
        d. Preexisting diseases that may exacerbate effects or contribute to synergistic effects
    2. Perform a physical exam. Pay special attention to actual and potential problems noted in the history. Record the patient´s height, weight, pulse, respiration rate, and blood pressure.
    3. Record the results of laboratory tests. At minimum, tests performed should be:
        a. CBC, blood-chemistry panel, urinalysis. (Urinalysis should be performed at least yearly, more often if results are abnormal.)
        b. Any tests that history, physical examination, or previous treatment suggests are necessary
    4. Imaging studies as indicated (e.g., chest x-ray)
    5. Function testing as indicated (e.g., pulmonary function tests, echocardiogram)

B. Collaborative management
    1. Coordinate follow-up visits with the oncologist, or refer the patient to his or her primary physician.
    2. Identify problems suggested by the history, physical exam, or test results. Develop a plan for medical intervention, follow-up, or referral.
    3. Coordinate consultation or referral to specialists if problems need management.
    4. Provide patient and family education
        a. Teach the importance of maintaining a treatment record and health diary.
        b. Remind the patient and family of the need to continue follow-up for life.
        c. Educate the patient and family about the potential problems related to cancer therapy.
        d. Encourage health-promoting practices: limiting fat intake and alcohol use, exercising regularly, and avoiding tobacco.
        e. Teach proper medication administration and the signs of potential side effects.
    5. Help the patient manage problems by using available resources and supplementing resources if necessary.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is cited throughout the body of the original guideline document.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

This guideline will provide the registered nurse with the clinical information necessary to safely prepare, store, transport, handle, administer, dispose of, and assess response to cytotoxic and biotherapeutic agents. In addition, it will prepare the nurse to be able to prevent and manage any adverse reactions, side effects, and toxicities associated with treatments.

POTENTIAL HARMS

Chemotherapy

- Hypersensitivity or anaphylactic reactions.
- Cardiotoxicity. Refer to Table 30 in the original guideline document for a list of cardiotoxic chemotherapeutic drugs by category.
- Pulmonary toxicity and hepatotoxicity. Refer to Table 32 in the original guideline document for a list of agents by classification that cause hepatotoxicity or pulmonary toxicity.
- Nephrotoxicity. Refer to Table 33 in the original guideline document for a list of nephrotoxic chemotherapeutic agents.
- Neurotoxicity. Refer to Table 35 in the original guideline document for areas of neurologic deficits that may be associated with specific chemotherapeutic agents.
- Alterations in sexuality and reproductive function. Refer to Table 36 in the original guideline document for a list of chemotherapeutic agents that affect sexual or reproductive function.
- Cutaneous reactions.
- Ocular toxicities. Refer to Table 39 in the original guideline document for a list of toxicities associated with chemotherapy.
- Secondary malignancies. Refer to Table 40 in the original guideline document for a list of secondary malignancies related to chemotherapy.

Refer to Table 4 in the original guideline document for a detailed list of side effects for specific cytotoxic agents.

Potential complications of antineoplastic agents by routes of administration:

- Oral. Drug-specific complications
- Subcutaneous intramuscular. Infection, bleeding.
- Intravenous (IV). Infection, phlebitis, extravasation
- Intra-arterial. Bleeding, embolism, pain
- Internal (implanted) pump. Pump occlusion malfunction, bleeding, embolism, pain
- Intrathecal intraventricular. Increased intracranial pressure, headaches, confusion, lethargy, nausea and vomiting, seizures, infection

- Intraperitoneal. Abdominal pain, distention, bleeding, ileus, intestinal perforation, infection
- Intravesicular. Urinary tract infections, cystitis, bladder contracture, urinary urgency

Biotherapy

- Potential side effects of biological response modifiers: alteration in hematologic lab value, alteration in mental status, anaphylaxis, anorexia, bone pain, bronchospasm, capillary leak syndrome, chills, desquamation, diarrhea, peripheral edema, pulmonary edema, fatigue, fever, fluid retention, flushing, headache, hives, hypotension, liver enzymes, mucositis, myalgia, nausea, pruritus, rash, tachycardia, weight loss, weight gain. Refer to Table 20 in the original guideline document for details as to the likelihood (i.e. common, occasional, rare) of these side effects.
- General side effects of biotherapy: hypotension, arrhythmia, capillary leak syndrome; dry desquamation, pruritus, transient flushing/flare reaction, alopecia; fever, chills or rigors (shaking chills), myalgia or arthralgia, headache, malaise, fatigue; nausea and/or vomiting, anorexia, diarrhea, stomatitis; neutropenia, thrombocytopenia, anemia; confusion or hallucinations, depression, anxiety, lethargy or somnolence, decreased concentration, insomnia, irritability, mood changes, peripheral neuropathy, dizziness, paresthesia, seizures or coma; respiratory symptoms (dyspnea, pulmonary edema, acute respiratory distress syndrome [ARDS], pleural effusion); elevated creatinine, blood urea nitrogen, and uric acid, oliguria. Refer to Table 5 in the original guideline document for a detailed list of side effects for each biologic agent.
- Refer to Table 39 in the original guideline document for a list of ocular toxicities associated with biotherapy.

Occupational Exposure to Cytotoxic Agents

Potential health risks to nurses and other personnel associated with occupational exposure to chemotherapeutic agents include carcinogenicity, genotoxicity, teratogenicity or fertility impairment, organ toxicity.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The guideline document is published by the Oncology Nursing Society (ONS). ONS neither represents nor guarantees that the practices described herein will, if followed, ensure safe and effective patient care. The recommendations contained in the guideline document reflect ONS´s judgment regarding the state of general knowledge and practice in the field as of the date of publication. The recommendations may not be appropriate for use in all circumstances. Those who use the guideline document should make their own determinations regarding specific safe and appropriate patient-care practices, taking into account the personnel, equipment, and practices available at the hospital or other facility at which they are located. The editors and publisher cannot be held responsible for any liability incurred as a consequence from the use or application of any of the

contents of these guidelines. Figures and tables are used as examples only. They are not meant to be all-inclusive, nor do they represent endorsement of any particular institution by the Oncology Nursing Society (ONS). Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Oncology Nursing Society.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Patient Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Oncology Nursing Society (ONS). Chemotherapy and biotherapy: guidelines and recommendations for practice. Pittsburgh (PA): Oncology Nursing Society (ONS); 2001. 226 p.

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2001

GUIDELINE DEVELOPER(S)

Oncology Nursing Society - Professional Association

SOURCE(S) OF FUNDING

Oncology Nursing Society

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Names of Group Members: Karen A. Brown, RN, PhD, AOCN; Peg Esper, MSN, RN, CS, AOCN; Linda O. Kelleher, RN, MS; Jill E. Brace O´Neill, MS, RN-CS, PNP; Marty Polovich, MN, RN, AOCN; Julie M. White, RN, BSN, OCN

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

Note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary.

GUIDELINE AVAILABILITY

Electronic copies: Not available at this time.

Print copies: Available for purchase from the Oncology Nursing Society, 125 Enterprise Drive, Pittsburgh, PA 15275-1214; telephone, 412-859-6100; fax, 412-859-6165.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

The following is available:

- Safe management of chemotherapy in the home. Appendix 2. In: Oncology Nursing Society (ONS). Chemotherapy and biotherapy: guidelines and recommendations for practice. Pittsburgh (PA): Oncology Nursing Society (ONS); 2001. 226 p.

Print copies: Available for purchase from the Oncology Nursing Society, 125 Enterprise Drive, Pittsburgh, PA 15275-1214; telephone, 412-859-6100; fax, 412-859-6165.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on May 8, 2003. The information was verified by the guideline developer on May 30, 2003. This summary was updated by ECRI on September 8, 2005 following the U.S. Food and Drug Administration (FDA) advisory on Herceptin (trastuzumab). This summary was updated by ECRI on February 7, 2006 following the Food and Drug Administration (FDA) advisory on Hydrea and Droxia (hydroxyurea capsules). This summary was updated by ECRI on March 24, 2006 following the FDA advisory on Ontak (denileukin diftitox).

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx.

NGC, AHRQ, and its contractor ECRI make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect

those of NGC, AHRQ, or its contractor ECRI, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 5/22/2006